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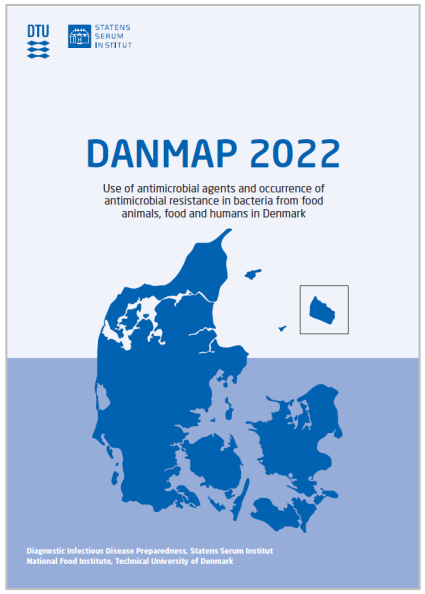
DANMAP

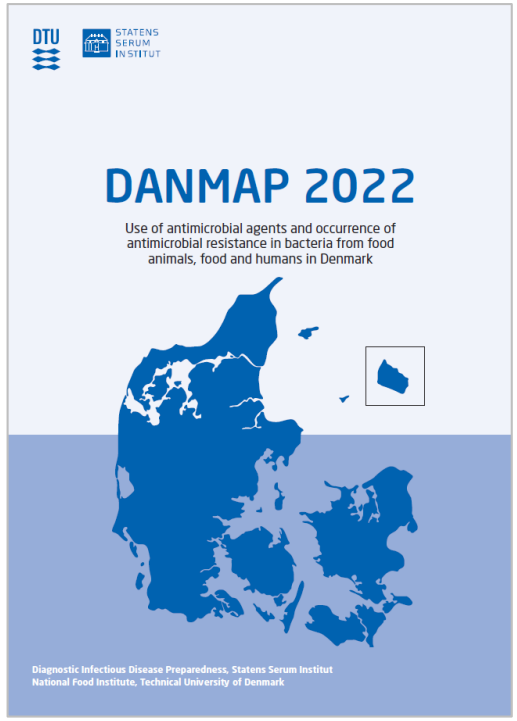
DANMAP Seminar

Danish Programme for surveillance of antimicrobial consumption and resistance in bacteria from food animals, food and humans



Agenda

- Antimicrobial consumption in animals
- Antimicrobial consumption in humans
- Antimicrobial resistance in zoonotic bacteria and indicator bacteria from animals and food
- Antimicrobial resistance in bacteria from humans
- Antimicrobial resistance in pathogenic bacteria from animals

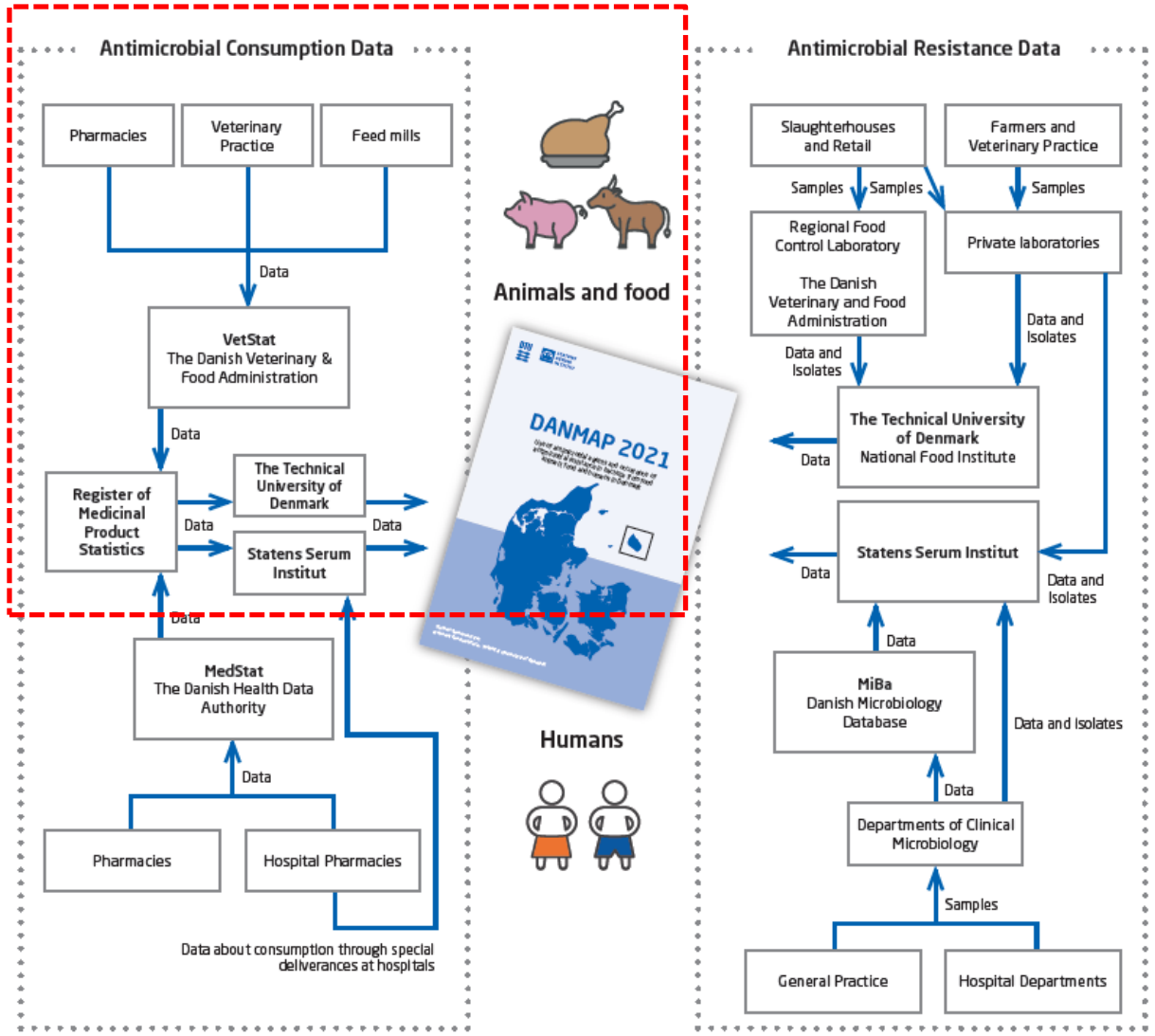


Antimicrobial consumption in animals

Vibe Dalhoff Andersen
Dyrlæge, Senior researcher, DTU Food

Marianne Sandberg
Dyrlæge, Senior researcher, DTU Food

DANMAP data flow



Text boxes in chapter 4 (Antimicrobial consumption in animals), DANMAP 2022

Textbox 4.1

No more high dose zinc oxide in veterinary medicinal products

Following a review of the safety and effectiveness of veterinary medicinal products containing zinc oxide to be administered orally to food-producing species, in the spring of 2017, the European Medicines Age
zinc oxide for the prevention of diarrhoea in pigs did not outweigh the risks for the e
mendations from EMA, the European Commission issued a decision on the 26th of Ju
authorisations. Member States could defer the withdrawal of the marketing authoris

Textbox 4.2

New EU legislation on veterinary medicinal products

cts has applied since 28 January 2022. The Order aims to reduce the administra-
d increase the availability of veterinary medicinal products, while guaranteeing
and environmental protection. There is a particular focus on reducing the risk of

tion on veterinary medicinal products (VMPs) is shared between the Danish Veteri-
e Danish Medicines Agency (DMA).

amework on the use of VMPs.

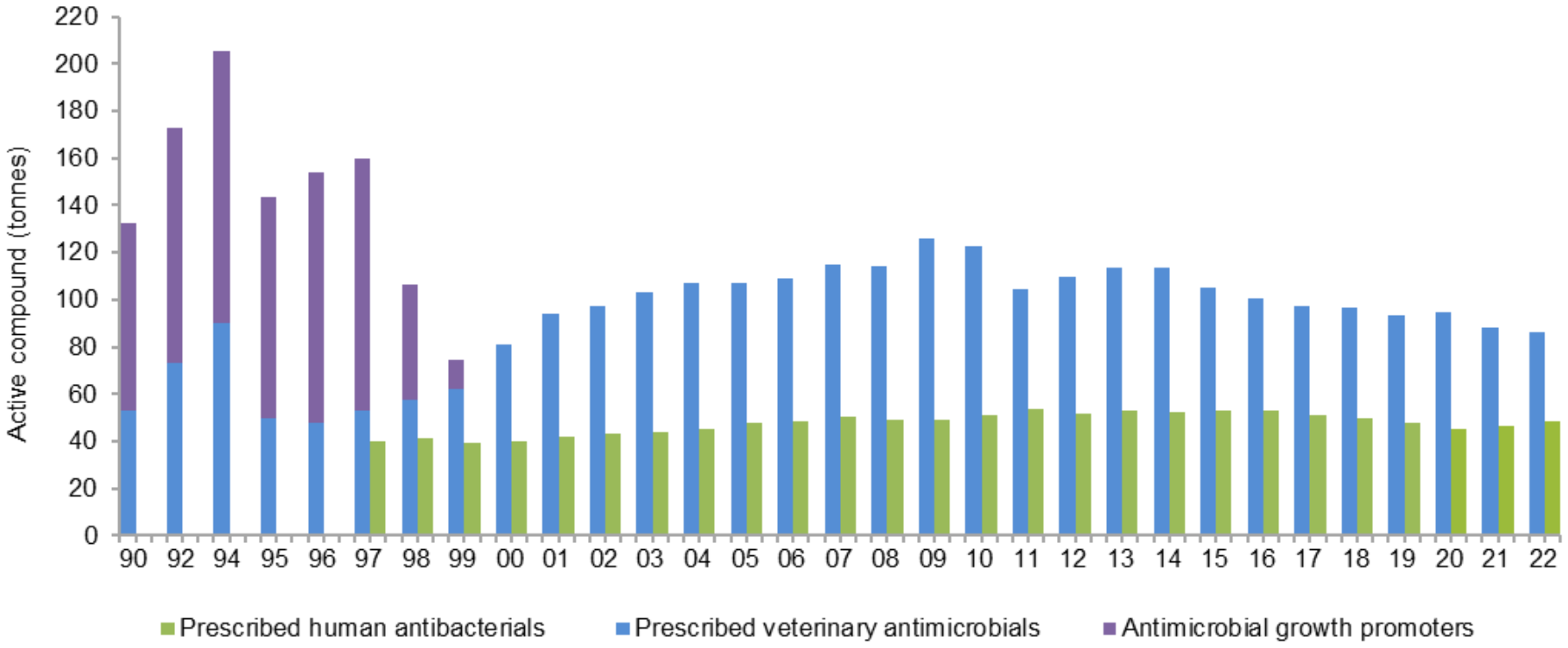
Textbox 4.3

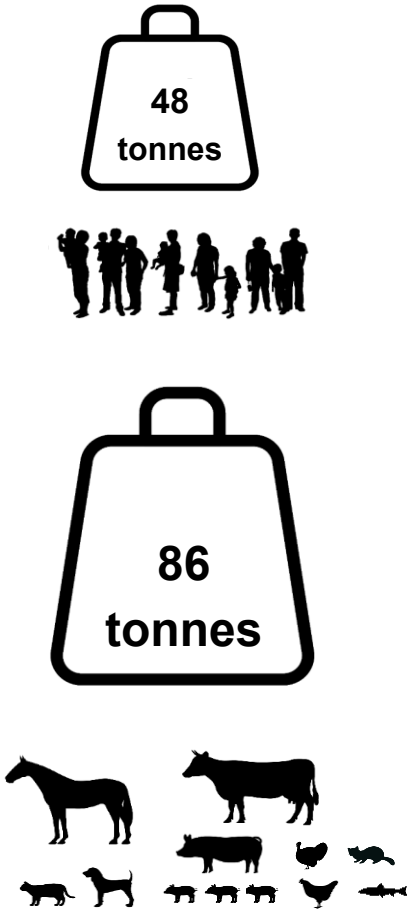
Faecal microbiota transplantation for prevention of diarrhoea in pigs

Background

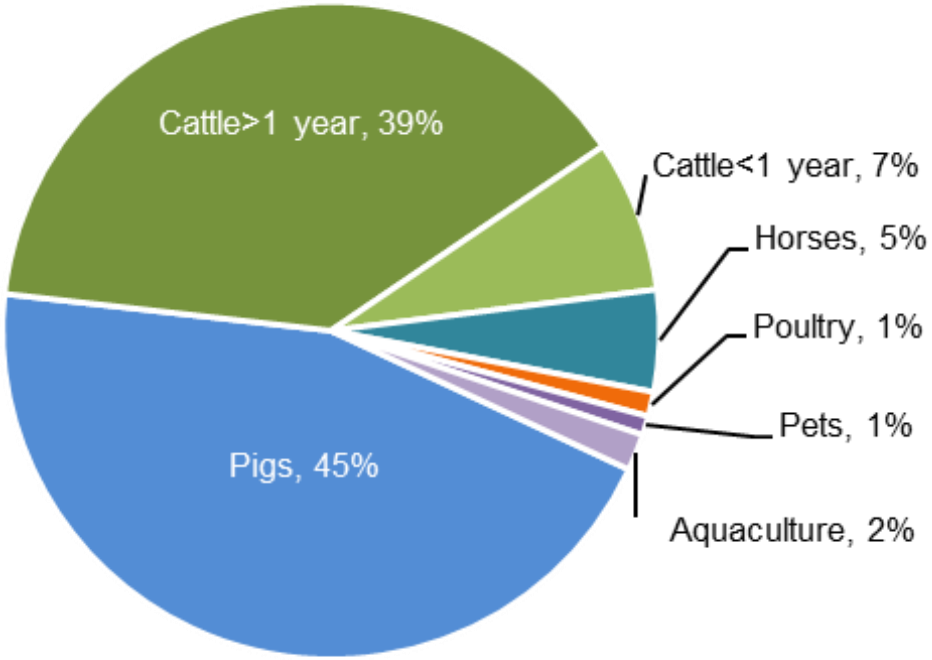
Faecal microbiota transplantation (FMT) is a medical procedure in which faecal material from a healthy donor is transplanted into the gastrointestinal tract of a recipient to restore a healthy microbial balance in the gut. The procedure is used in human medicine to treat certain gastrointestinal disorders associated with an imbalance of the gut microbiota, particularly recurrent *Clostridioides difficile* infection [1]. In veterinary medicine, transplants of faeces or ruminal fluid have been used in horses and cows to restore the gastrointestinal microbiome after antibiotic treatment. In pigs there is experimental evidence that transplants of intact faeces or faecal filtrates can be used to colonize the gut immediately after birth [2-3]. As part of the EU project AVANT (https://avant-project.eu/), which is coordinated by the University of Copenhagen, FMT and other alternatives

Antimicrobial consumption in animals and humans – a historical overview

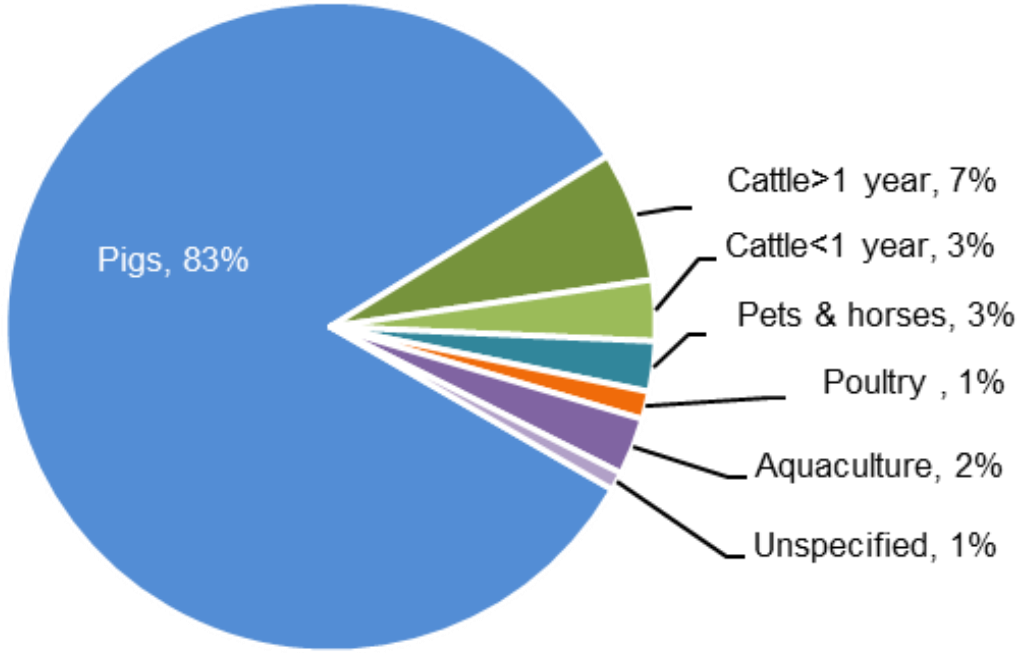




Relative distribution of biomass and antimicrobial consumption, animals, 2022

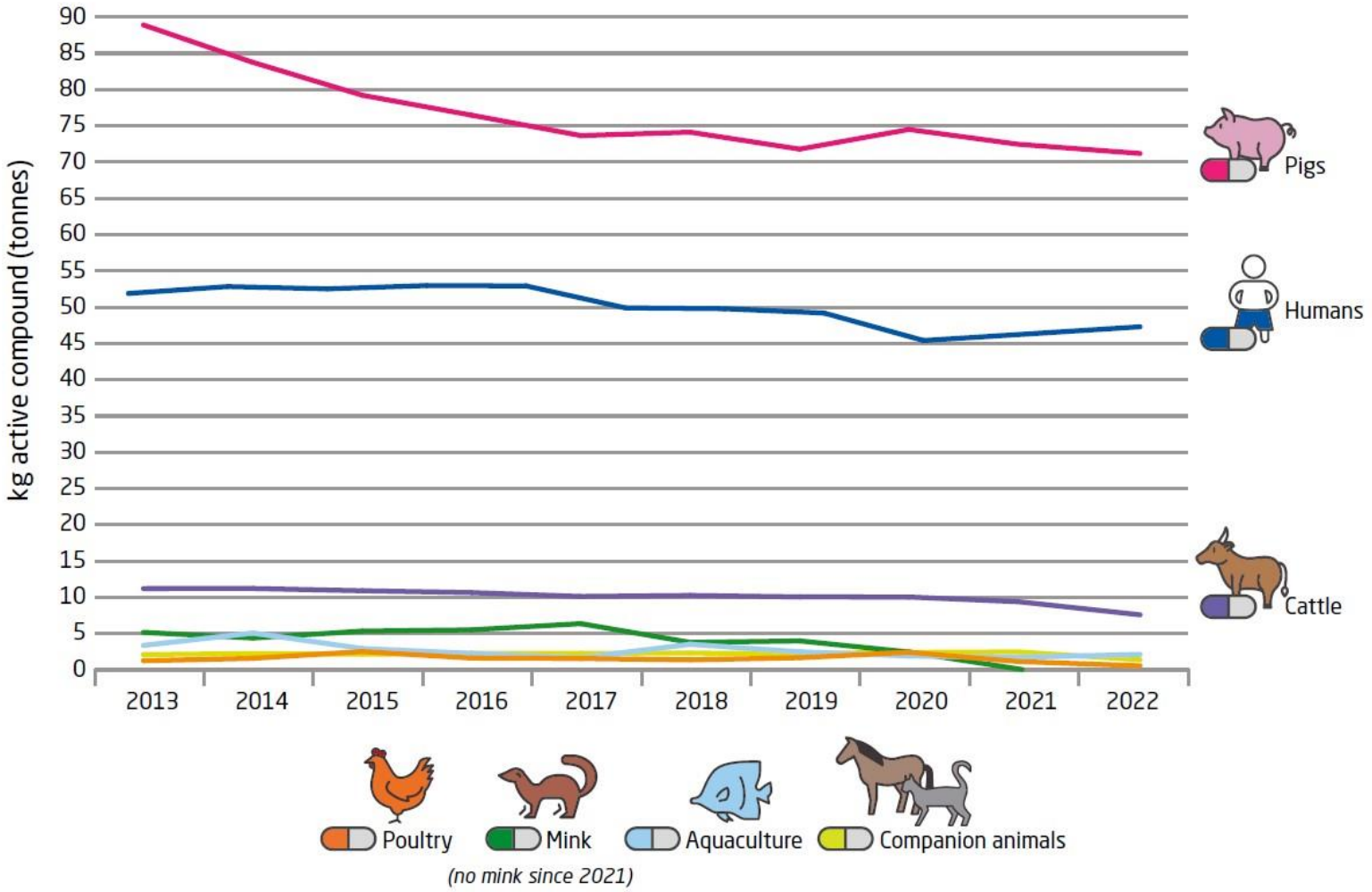


Biomass



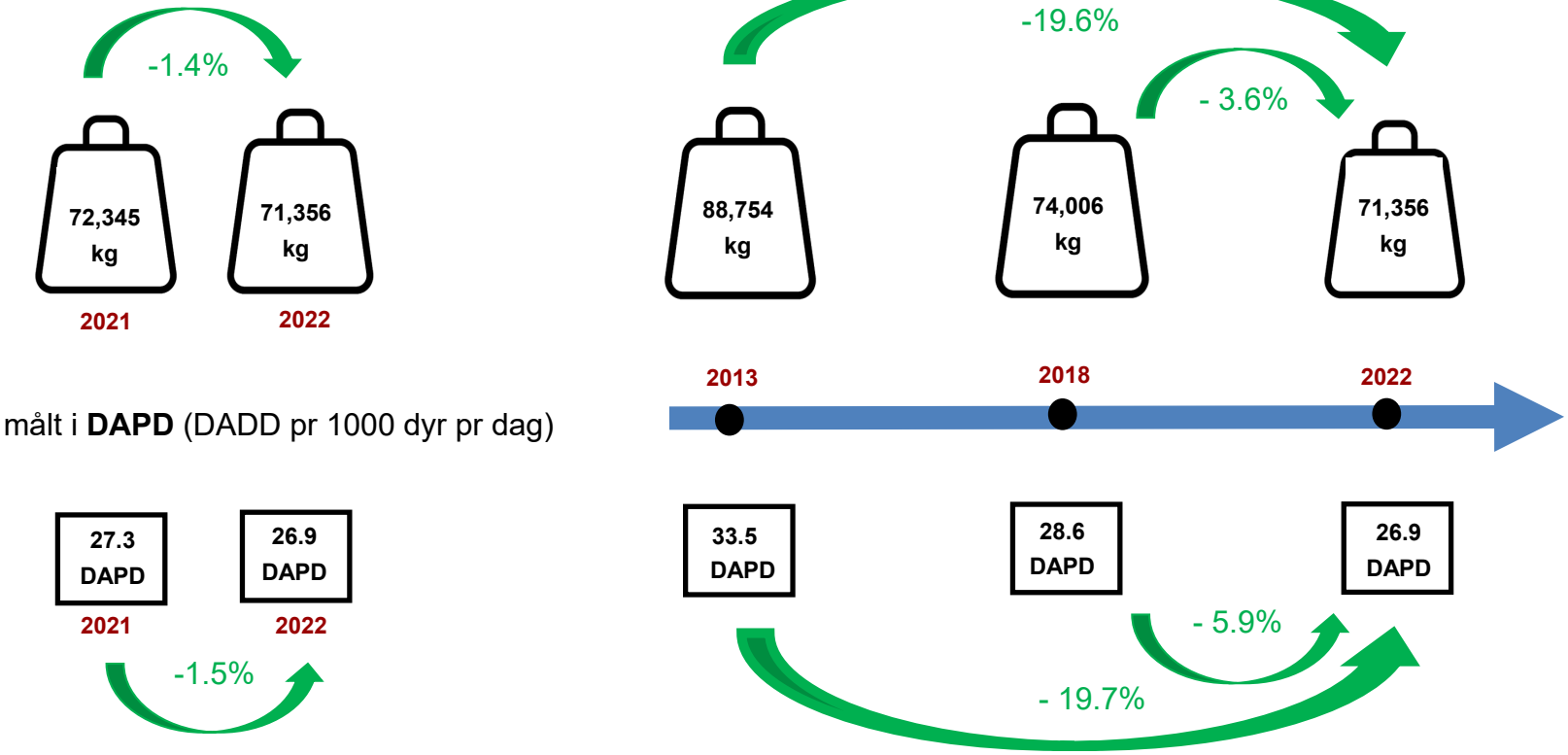
Active compound

Antimicrobial consumption in animals and humans, 2013-2022



Small amounts of kg active compound were used by unspecified animal species in 2022

Units for antimicrobial consumption – kg active compound & treatments of pigs



10 DAPD corresponds to that 1% of the pig population is treated on a given day

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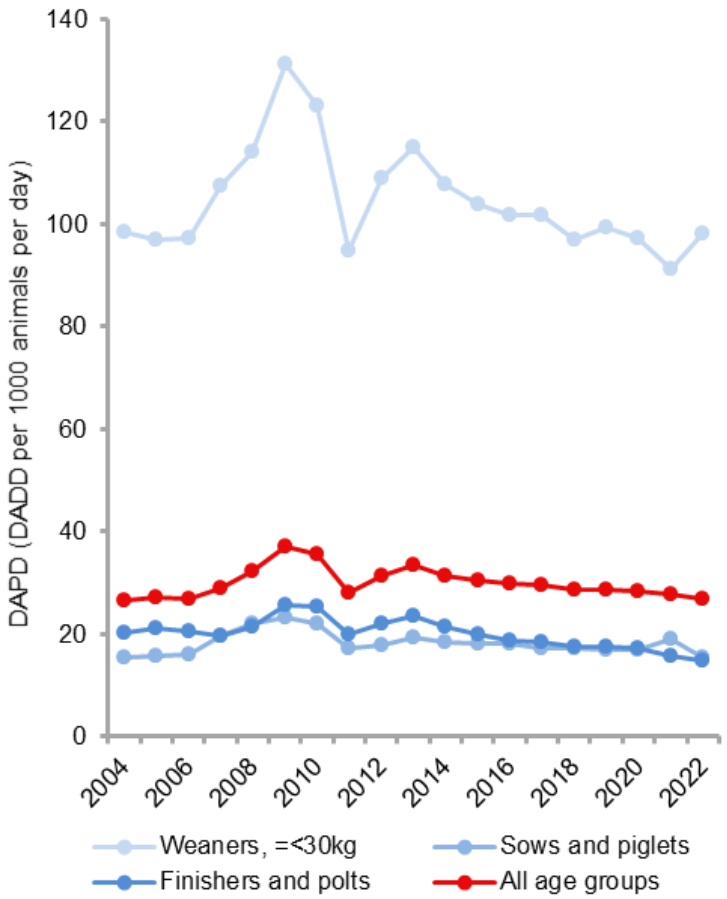
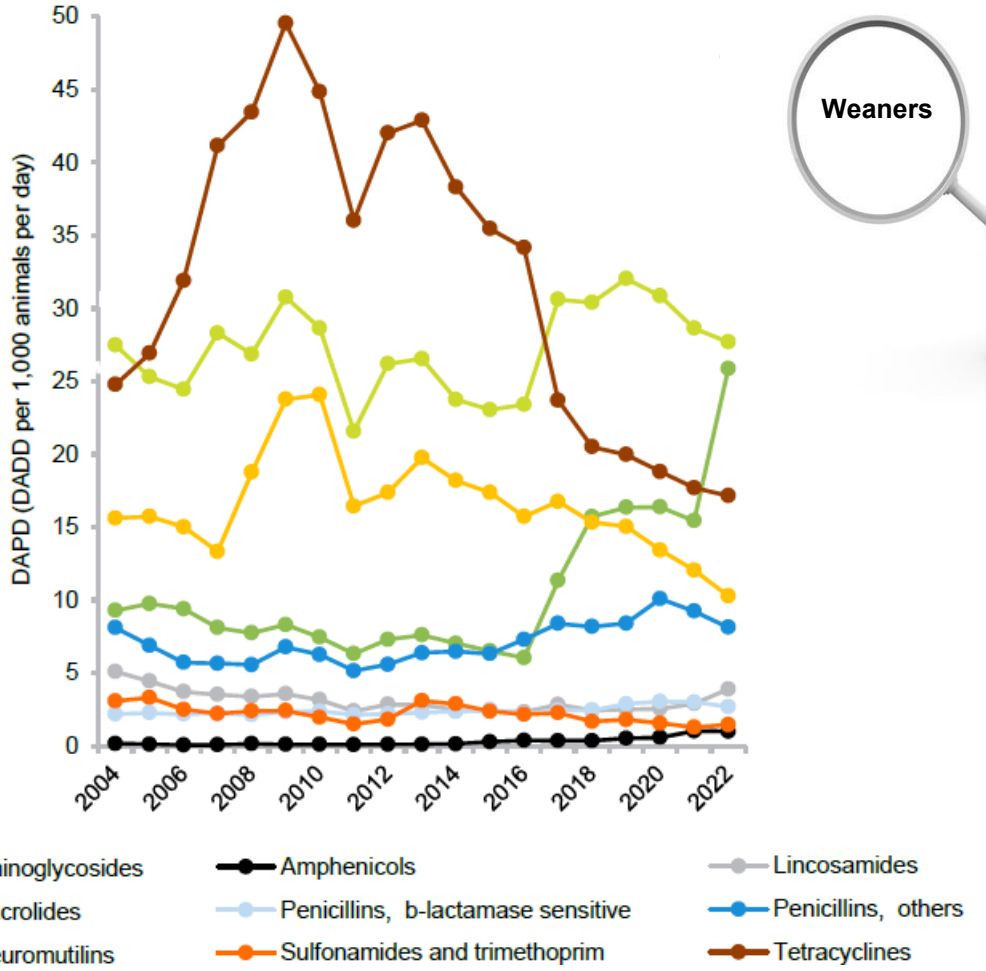
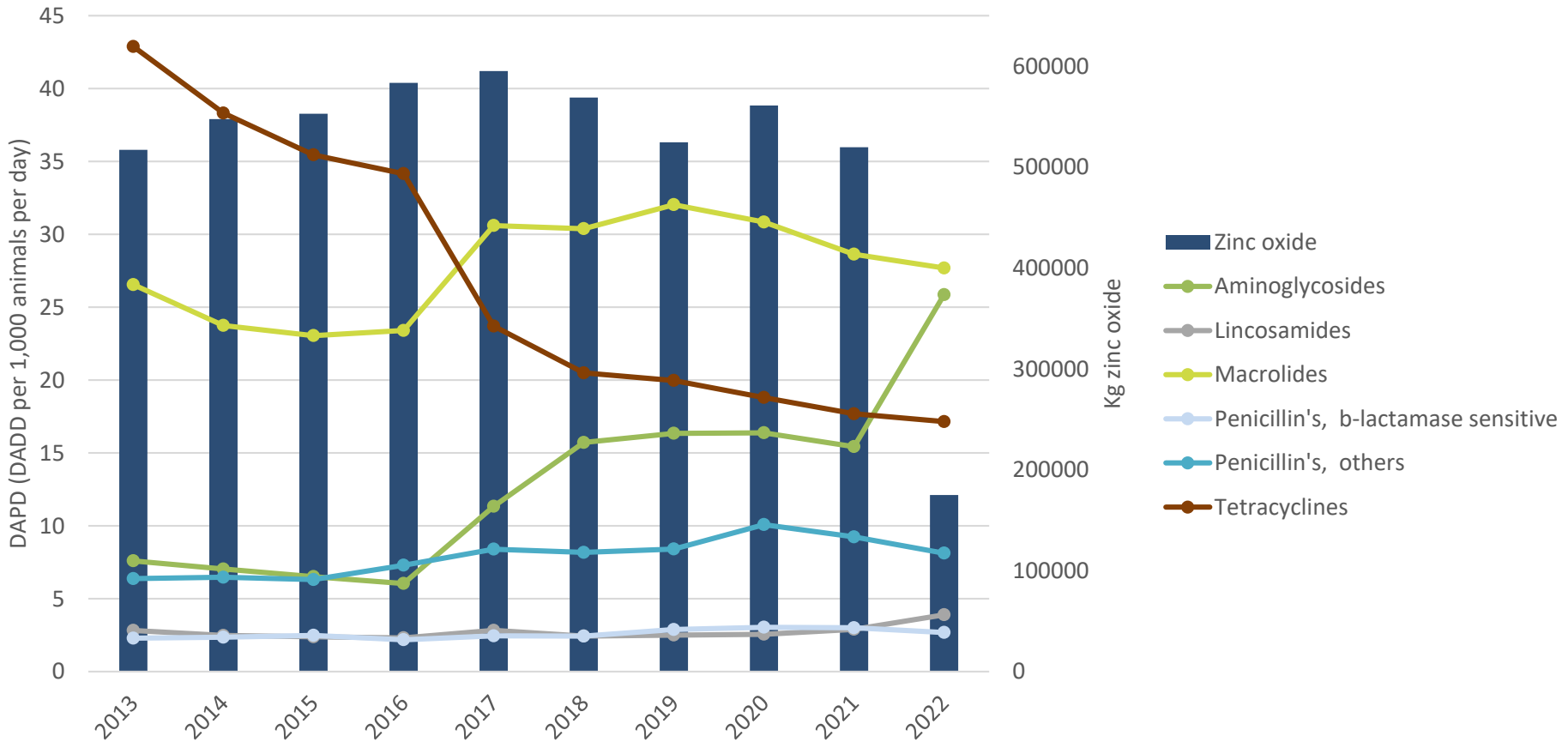
Consumption of antimicrobials in pigs





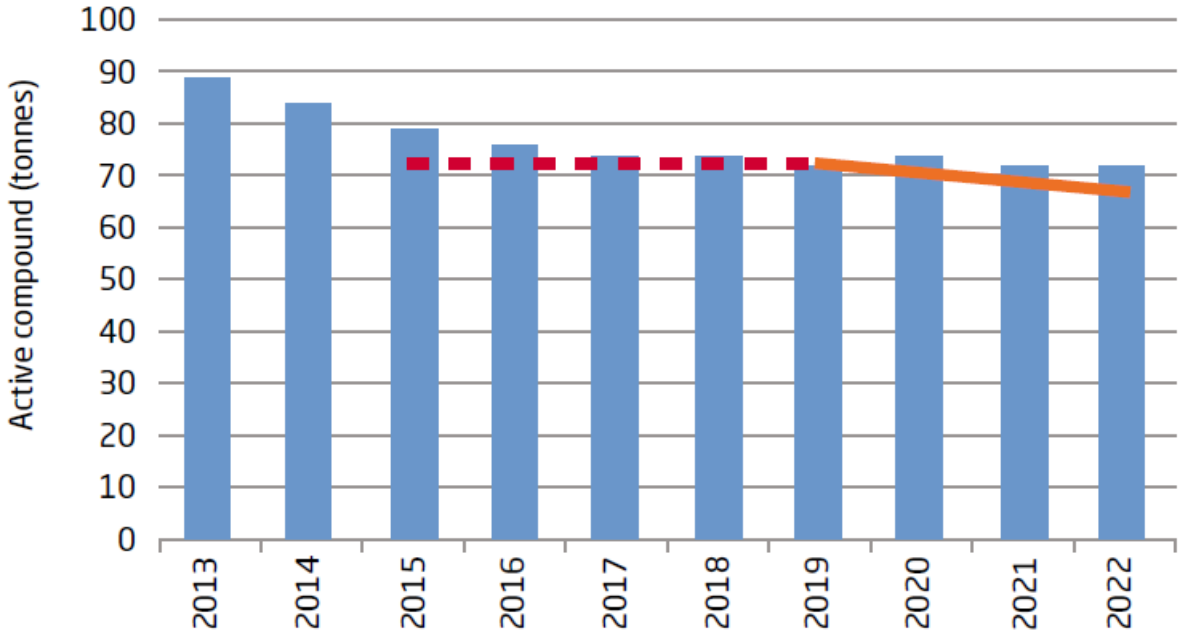
10 DAPD corresponds to that 1% of the pig population is treated on a given day

Antimicrobial (DAPD) and zinc oxide (kg) consumption in weaners, Denmark, 2013-2022



10 DAPD corresponds to that 1% of the pig population is treated on a given day

Action Plan – target for reduction of antimicrobial consumption in pigs



Goal 2015-2018

Goal 2019-2022
(extended to 2023)

Fødevarestyrelsens handlingsplan
mod
antibiotikaresistens

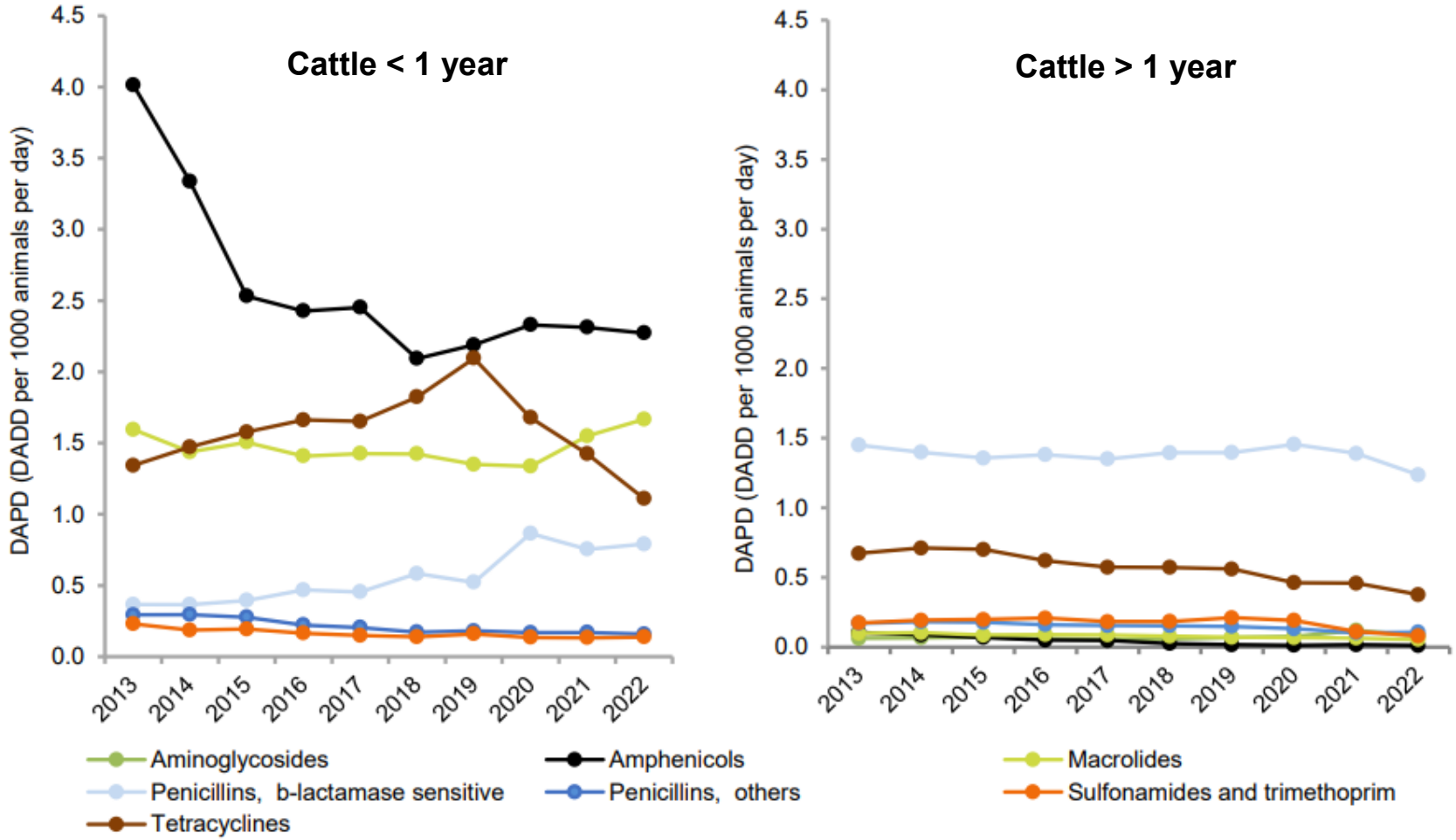
2017

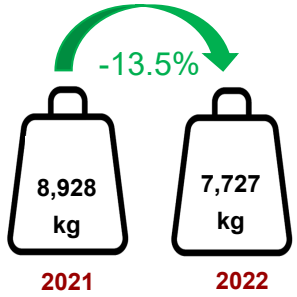
Ministeriet for Fødevarer,
Landbrug og Fiskeri
Fødevarestyrelsen

Fødevarestyrelsens nationale handlingsplan for antibiotikaresistens hos produktionsdyr og i fødevarer 2021-2023

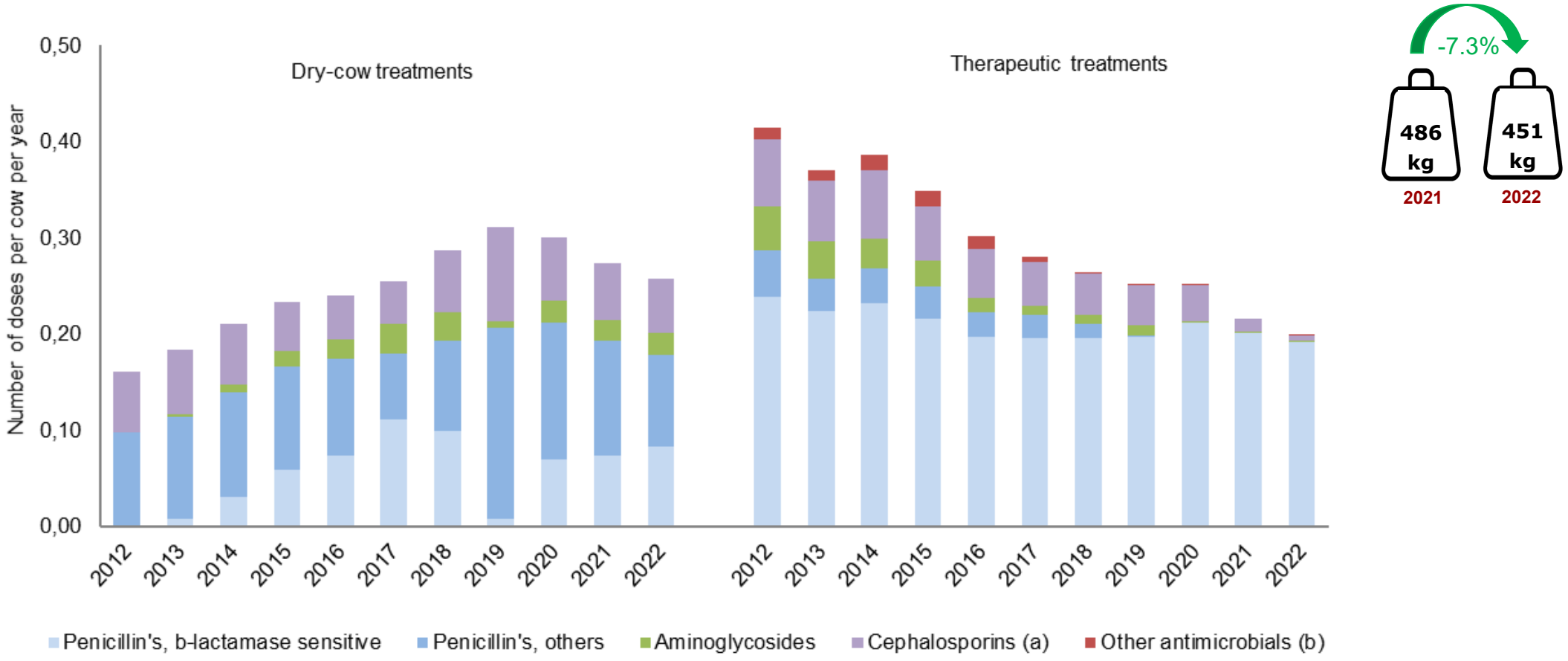
Danmark, Glostrup august 2021

Antimicrobial consumption in cattle, systemic use

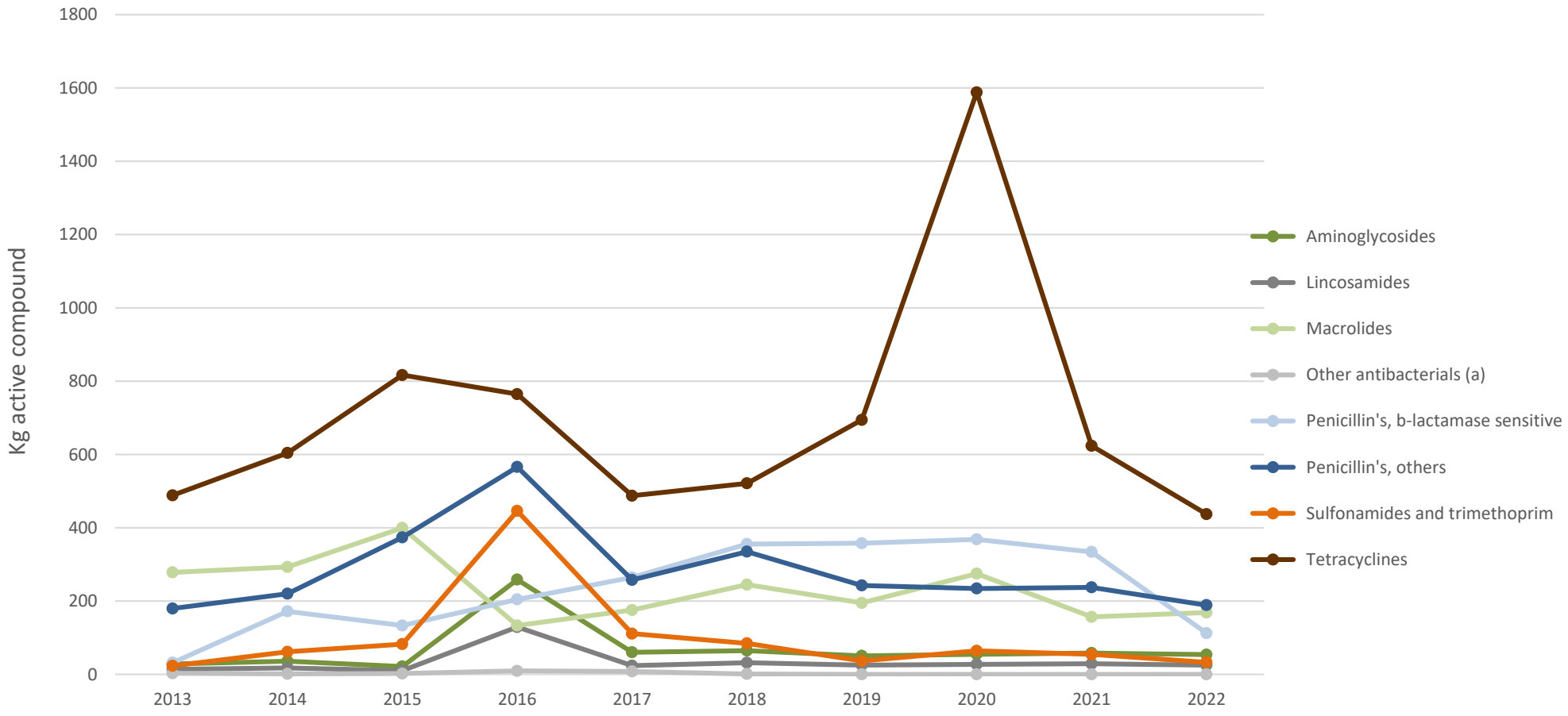




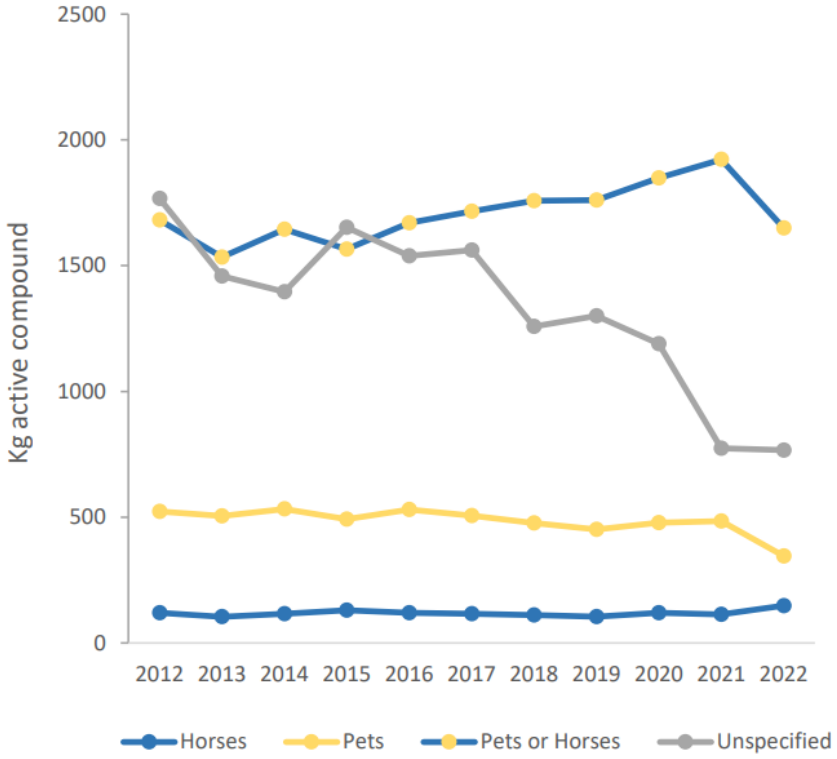
Antimicrobial consumption in cattle, intramammaries



Consumption of antimicrobials in poultry



Consumption of antimicrobials in companion animals, horses and unspecified



- The consumption for companion animals was estimated to be 2,143.3 kg in 2022, which was the same as in 2013 and 14.9% lower than in 2021
- More than half of all cephalosporins, all 3rd and 4th generation cephalosporins, as well as close to all fluoroquinolones prescribed for veterinary use, were prescribed for companion animals

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Thanks

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Agenda

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- Antimicrobials in primary health care
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- Antimicrobials in hospitals
- International surveillance of antimicrobials
- Take-home message

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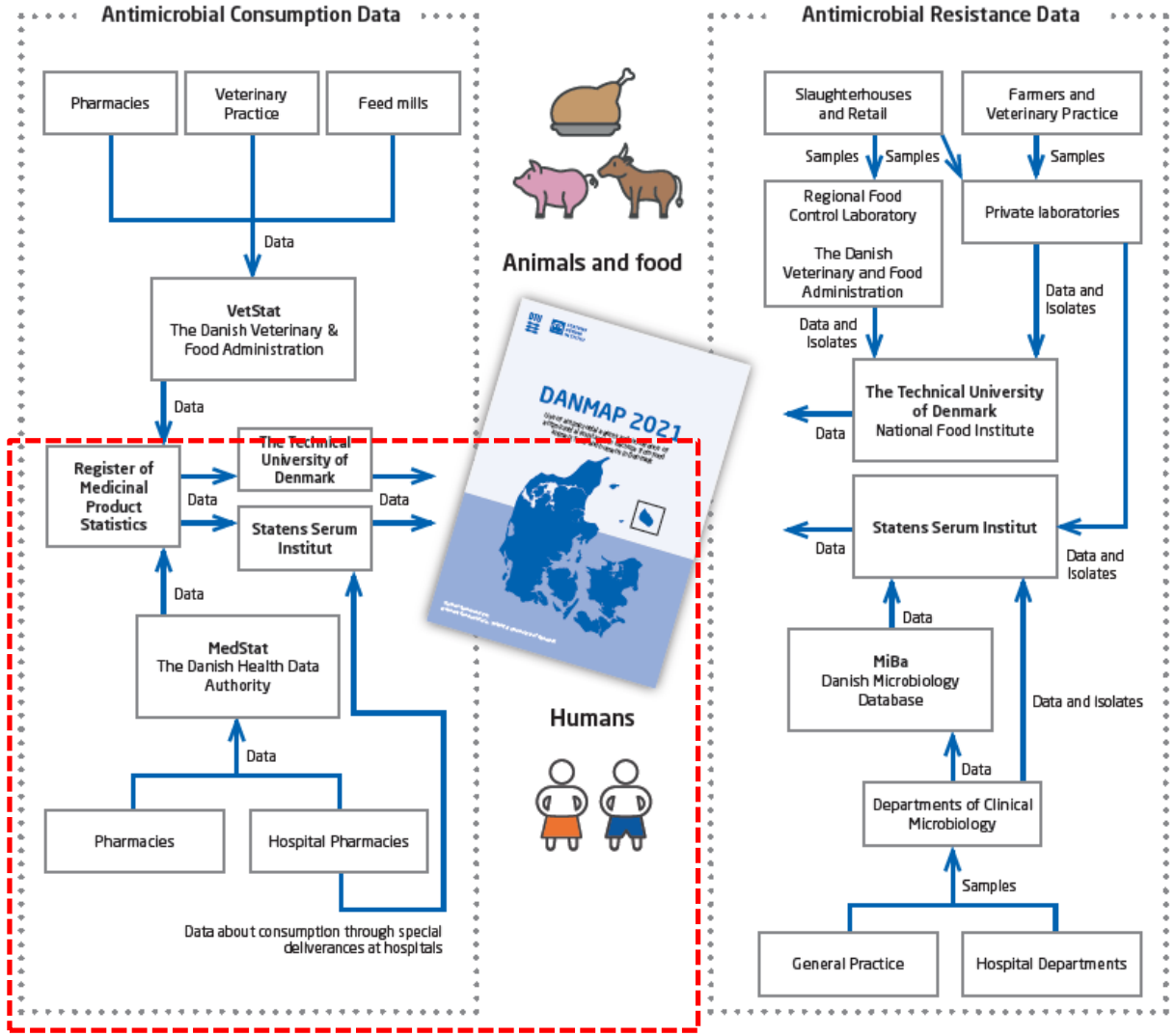
DANMAP data flow



Consumption is counted by several means

Number of prescriptions

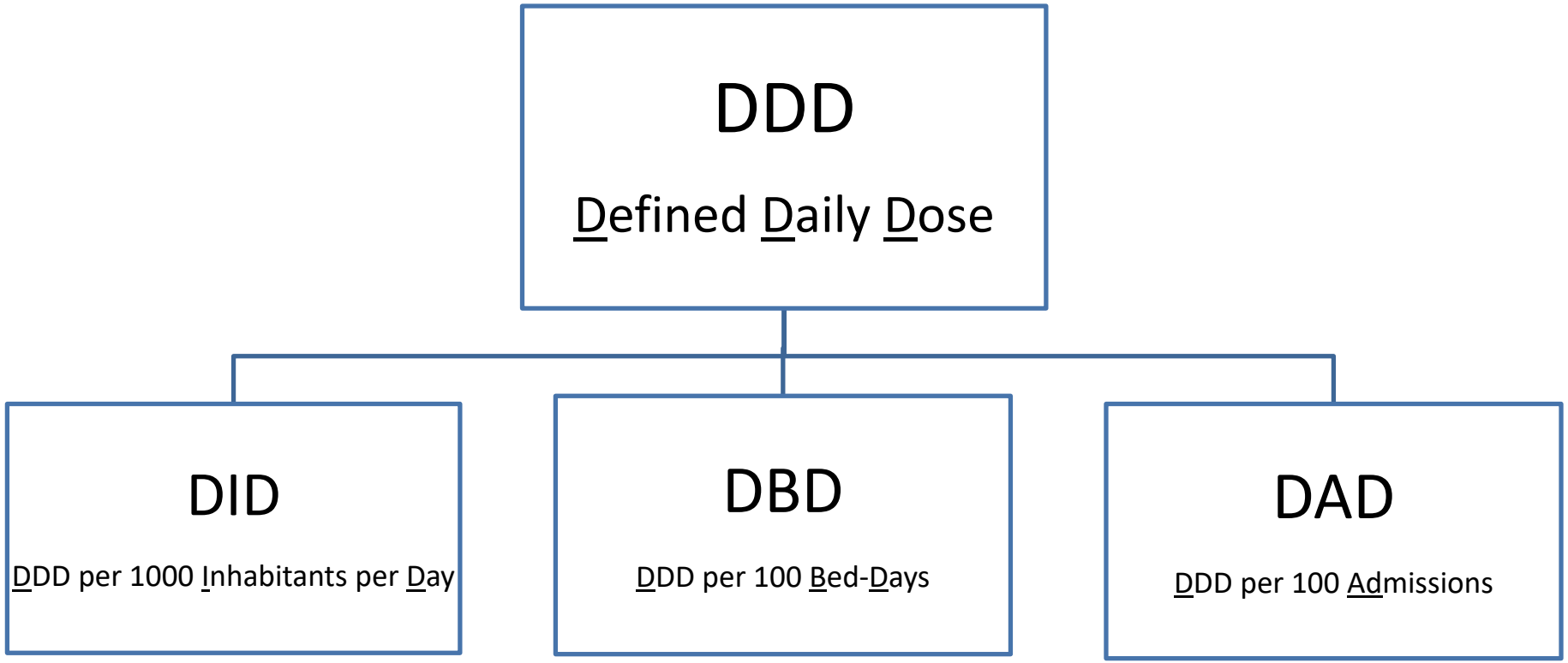
Number of treated patients

Defined daily doses (DDD)

> The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults

World Health Organization

Consumption units



Agenda

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DANMAP textboxes

Textbox 5.1

Comparison of antibiotic prescribing for elderly in long-term care facilities and elderly living at home

Background
Elderly people of 75 years and above are the age group that receive most antibiotics in Denmark. Urinary tract infection is the main indication. Antibiotic prescribing for this population was studied by comparing the use among elderly living in long-term care facilities and elderly living at home. Special attention was paid to the difference in prescribing antibiotics for urinary tract infection.

Methods
The study was observational and registry-based, and included all elderly Danish residents aged ≥ 75 years in 2016. Total antibiotic prescription rates were examined by including all antibacterial agents for systemic use (ATC J01). Prescription rates for urinary tract infection included pivmecillinam (ATC J01CA08), sulfamethizole (ATC J01EB02), trimethoprim (ATC J01EA01), nitrofurantoin (ATC J01XE01) and amoxicillin (ATC J01CA04). Antibiotic prescribing data were retrieved from the Danish Na-

Hadir Azaizi, Maria Louise Veimer Jensen, Ida Scheel Rasmussen, Jens Otto Jarløv and Jette Nygaard Jensen

Textbox 5.2

Sociodemographic characterisation of antibiotic heavy users in the Danish elderly population

Background
Elderly people (≥65 years) have the highest use of antibiotics and studies have shown an overuse within this population (1-3). Sociodemographic inequality is a well-known problem in health care, but it is not known whether sociodemographic factors also influence antibiotic use among Danish elderly people. The aim of this study was to investigate whether sociodemographic factors were associated with an excess use of antibiotics (i.e., being an antibiotic heavy user) in general practice among elderly people in Denmark.

Jette Nygaard Jensen and Maria Louise Veimer Mandrup of 65

Textbox 5.3

Incidence of multiresistant bacteria and consumption of antimicrobial agents in Greenland

Background
Greenland has a population of 56.562 inhabitants (January 2022, StatBank Greenland) and Nuuk is the capital with 19.261 inhabitants (January 2022, StatBank Greenland). Greenland has its own Ministry of Health and the country is divided into five health regions. There are five smaller hospitals, one national hospital and 11 health care centres in the five health regions. The national and largest hospital Dronning Ingrids Hospital (182 beds), is situated in Nuuk. Around 15-16,000 persons are admitted to hospital once or several times a year. Patients with specific or serious diseases which cannot be treated at Dronning Ingrids Hospital (DHI) are transferred to Denmark or Iceland, e.g. haemodialysis, cancer treatment, brain surgery etc.

Resistant bacteria
From 2000 to 2022, 129 patients have been diagnosed with methicillin-resistant *Staphylococcus aureus* (MRSA), 195 patients with extended spectrum beta-lactamase (ESBL)-producing *Enterobacterales*, four patients with vancomycin-resistant enterococci (VRE), and 217 patients with *Clostridium difficile* infection.

Anne Kjerulf, Anne Birgitte Jensen, Peter Poulsen and Camilla Møbjerg Andersen

Textbox 5.4

Shortage of antibiotics at Community Pharmacies in Denmark

The Association of Danish Pharmacies is the employer and professional organization of community pharmacies in Denmark. The association's Executive Board has the overall responsibility for the association's activities covering member services and promoting community pharmacy professional health services as an integrated part of the health care sector.

In Denmark, legislation obliges pharmacies to offer patients the cheapest, generic product of the prescribed medicine - also known as generic substitution. The legislation requires these substitutional products to have the same active component, formulation, strength, and same or smaller package size to ensure the same pharmaco-dynamics and -kinetics as the originally prescribed product. Antibiotics are allocated in dispensing group 'B' which means that package size is allowed to differ by up to 25% from the prescribed package size.

Per Nielsen, Head of Analysis and Julie Engelmann Mollerup, Health Consultant, cand.pharm

Textbox 5.5

Research Units for General Practice in Denmark

In Denmark, about 75% of antibiotics for human use are prescribed in general practice - mostly for infections related to the respiratory- and urinary tract systems. Also eye, skin, gastro-intestinal and sexually transmitted infections, among others, are treated with antibiotics in general practice.

Many patients present with viral, self-limiting infections; however, some do have serious, bacterial infections - in need of antibiotic treatment.

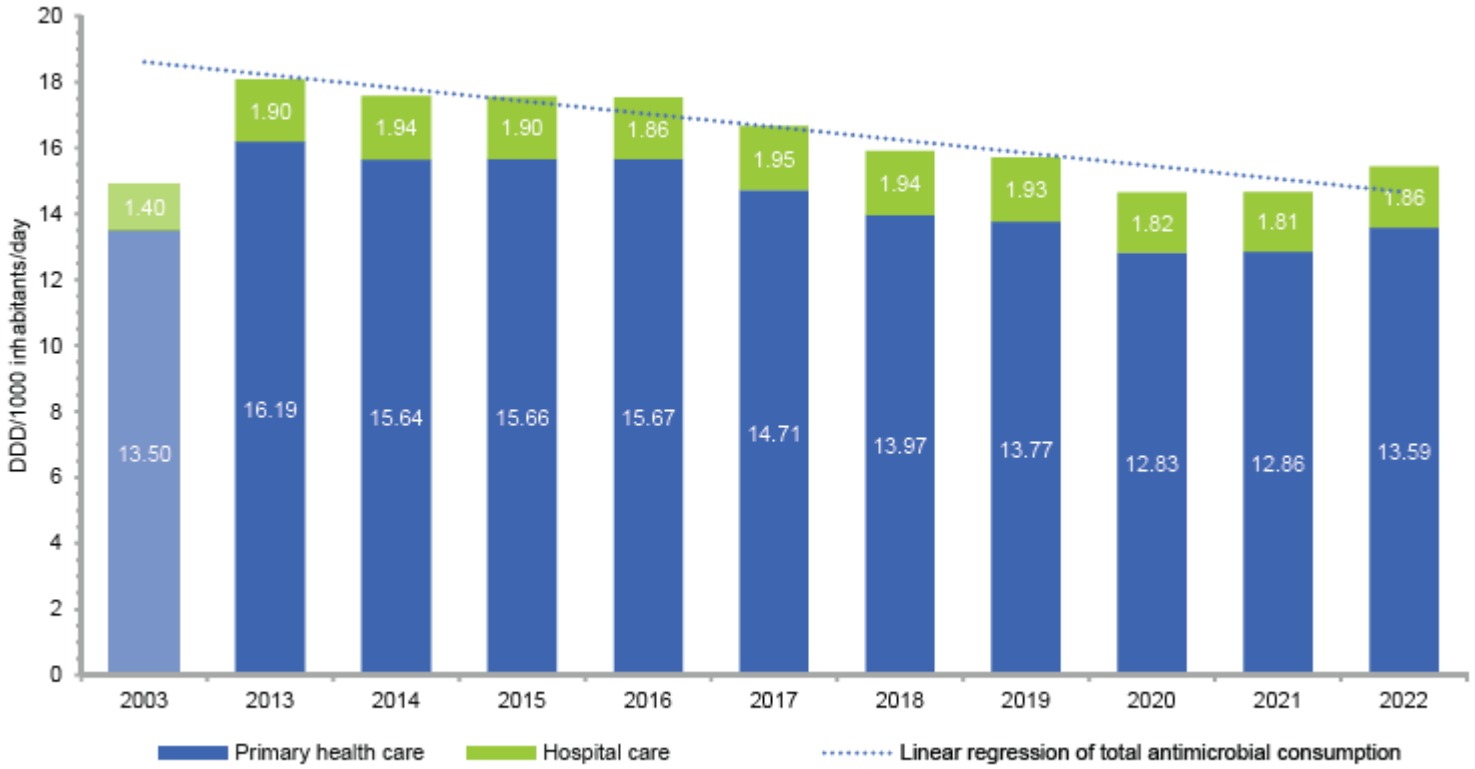
Research on antibiotic use
It can be challenging to find the "needle in the haystack" and no doubt both under- and overtreatment with antibiotics occur in

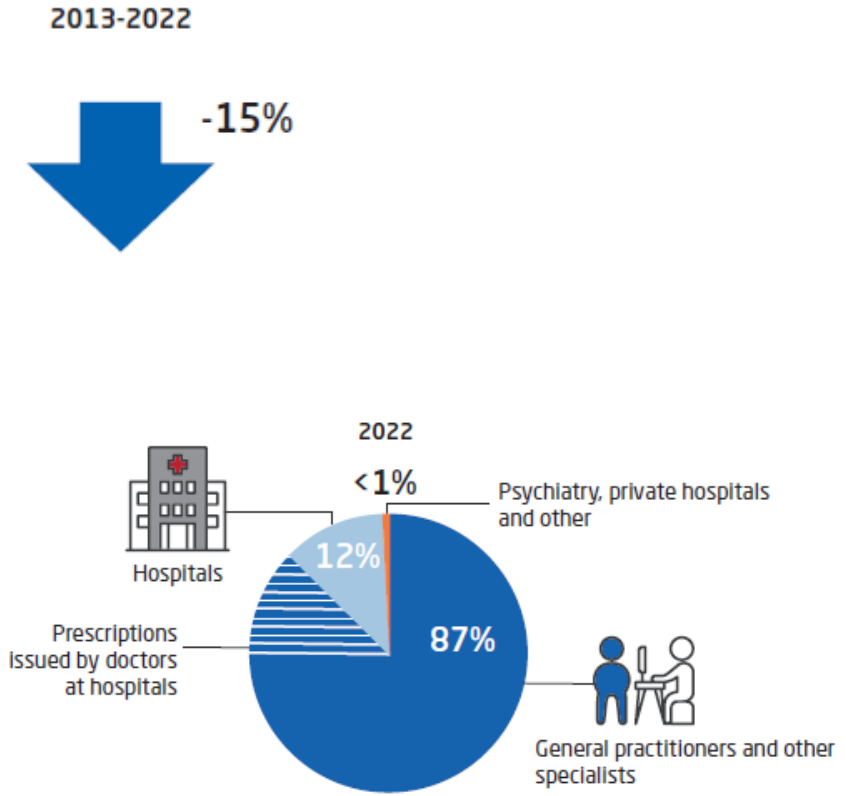
Malene Plejdrup Hansen

Antimicrobials in Denmark

Figure 5.1 Total consumption of systemic antimicrobial agents in humans, DDD per 1,000 inhabitants per day, Denmark, 2003 and 2013-2022

DANMAP 2022





Data: Total sale of antimicrobials in Denmark
Data source: Register of Medicinal Product Statistics and 2023 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Agenda

- Surveillance methodology
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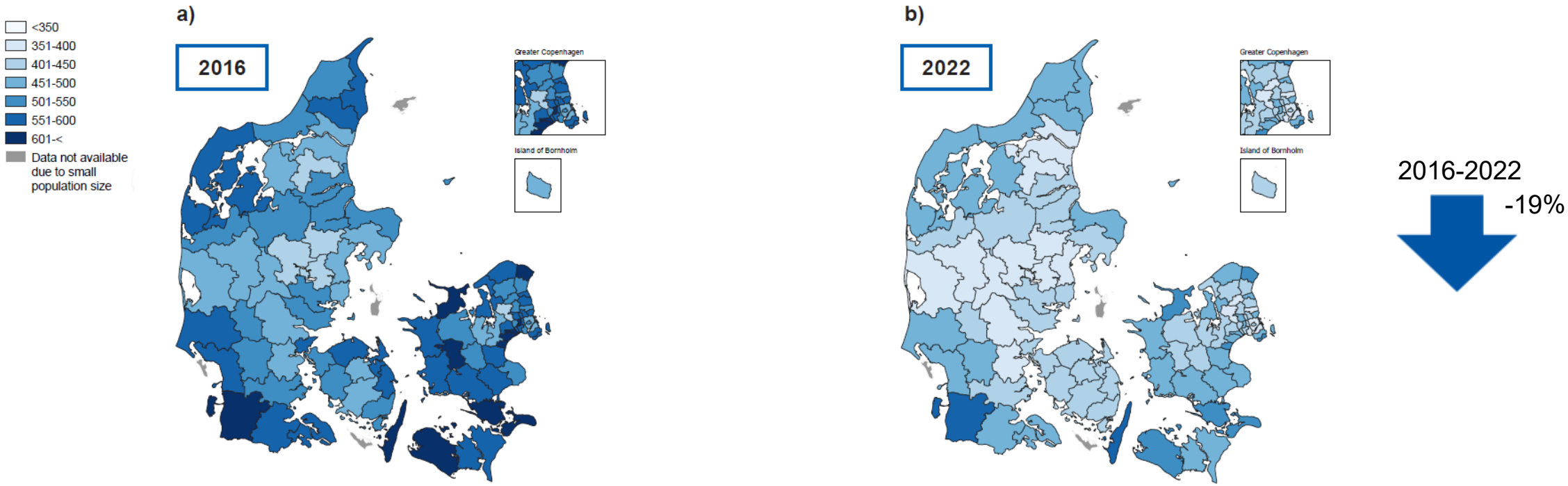
- Take-home message

Antimicrobials in primary health care

Figure 5.7 Number of prescriptions from primary health care per 1,000 inhabitants in Danish municipalities in a) 2016 and b) 2022

DANMAP 2022

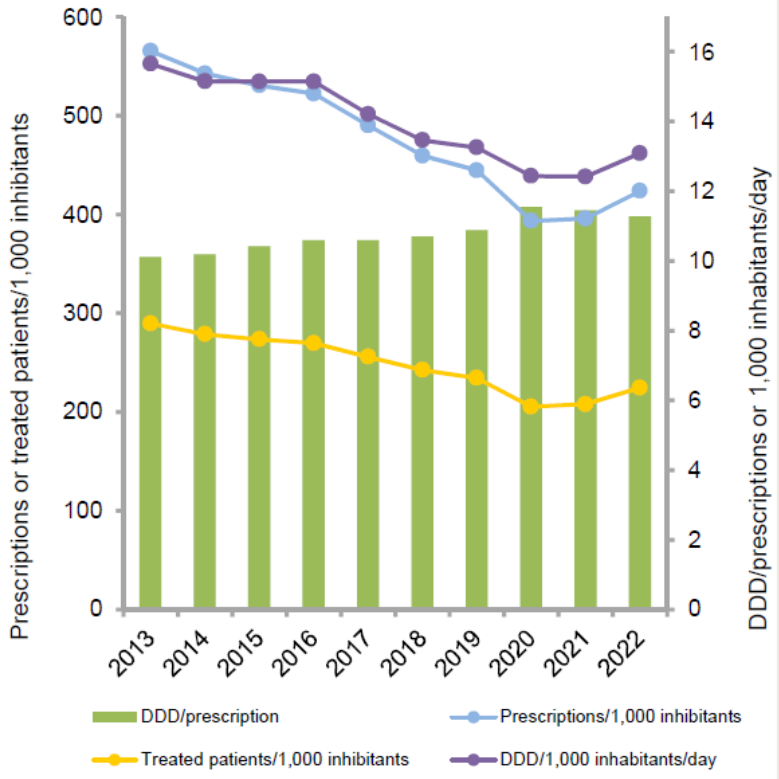


Data: Registered sale of antimicrobials to individuals

Data source: Register of Medicinal Product Statistics and 2023 edition of the Anatomical Therapeutic Chemical (ATC) classification system

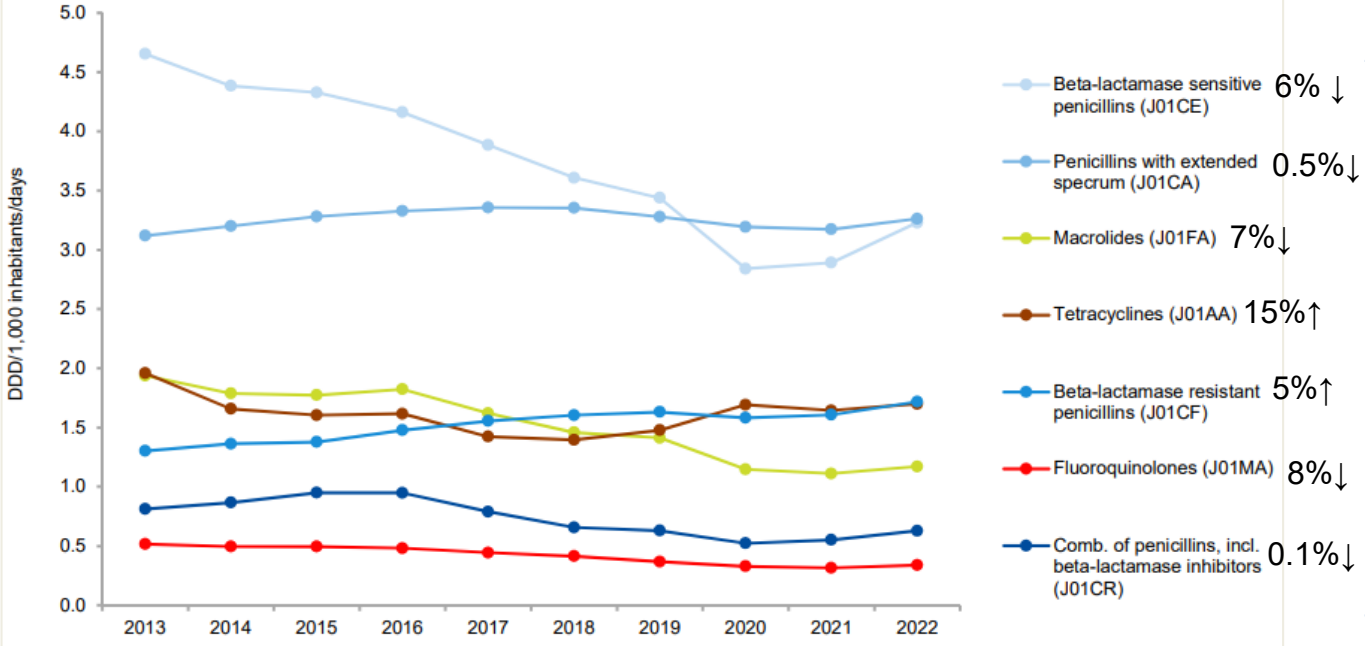
Antimicrobials in primary health care

Figure 5.5 Consumption of systemic antimicrobial agents in primary health care, Denmark, 2013-2022 DANMAP 2022



Data: Registered sale of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and 2023 edition of the Anatomical Therapeutic Chemical (ATC) classification system

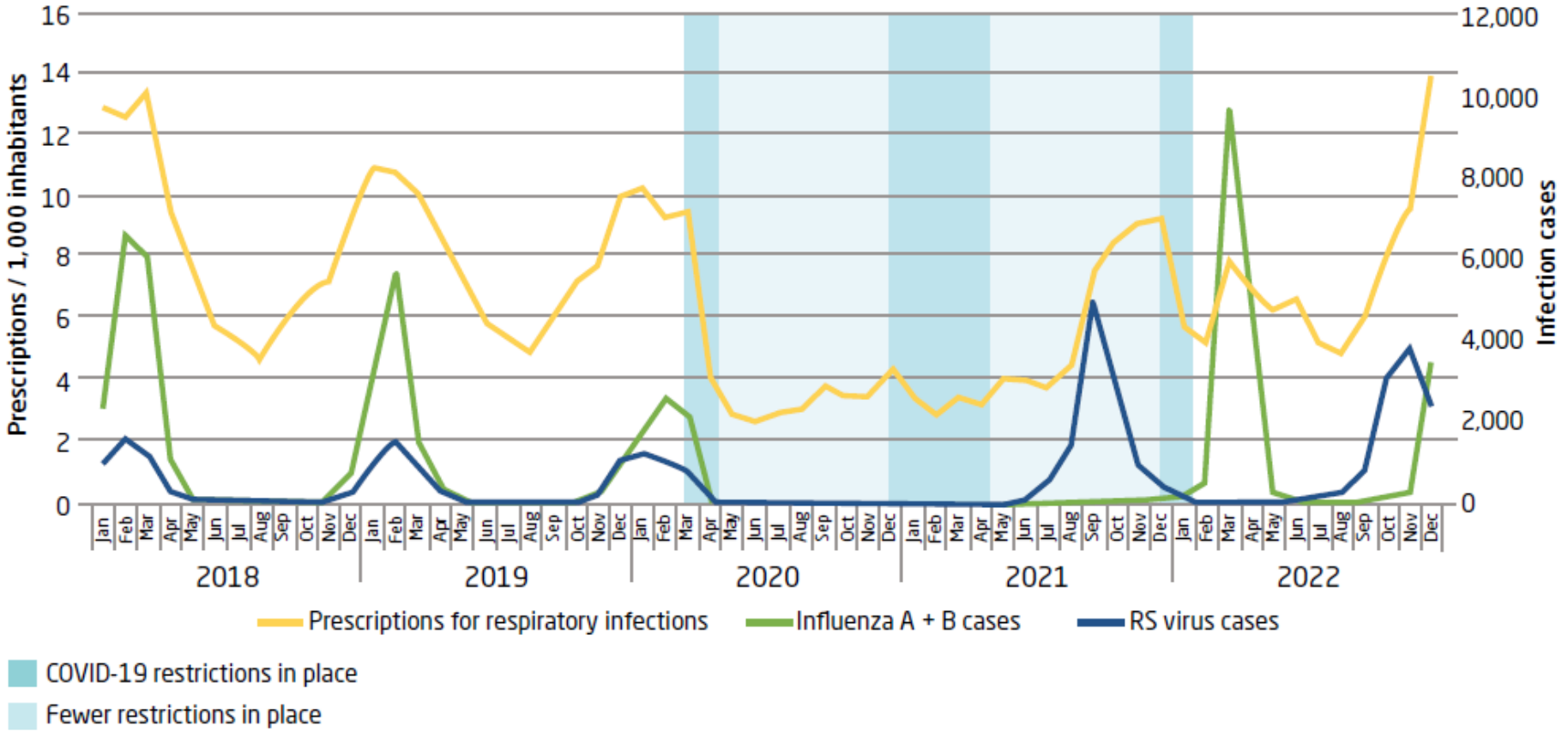
Figure 5.6 Consumption of leading antimicrobial groups for systemic use in primary health care, DDD per 1,000 inhabitants per day, Denmark, 2013-2022 DANMAP 2022



Data: Registered sale of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and 2023 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Antimicrobials for respiratory tract infections

Figure 3.2 Monthly consumption of systemic antimicrobials for the treatment of respiratory tract infections in primary health care, prescriptions per 1,000 inhabitants, and monthly number of laboratory confirmed influenza A and B as well as Respiratory Syncytial Virus (RSV), Denmark, 2018-2022



Agenda

- Methodology
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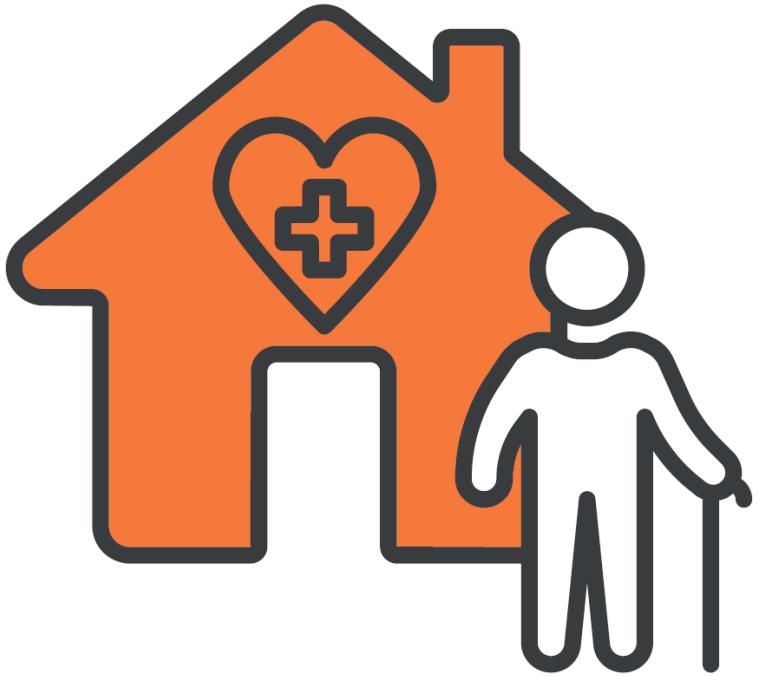
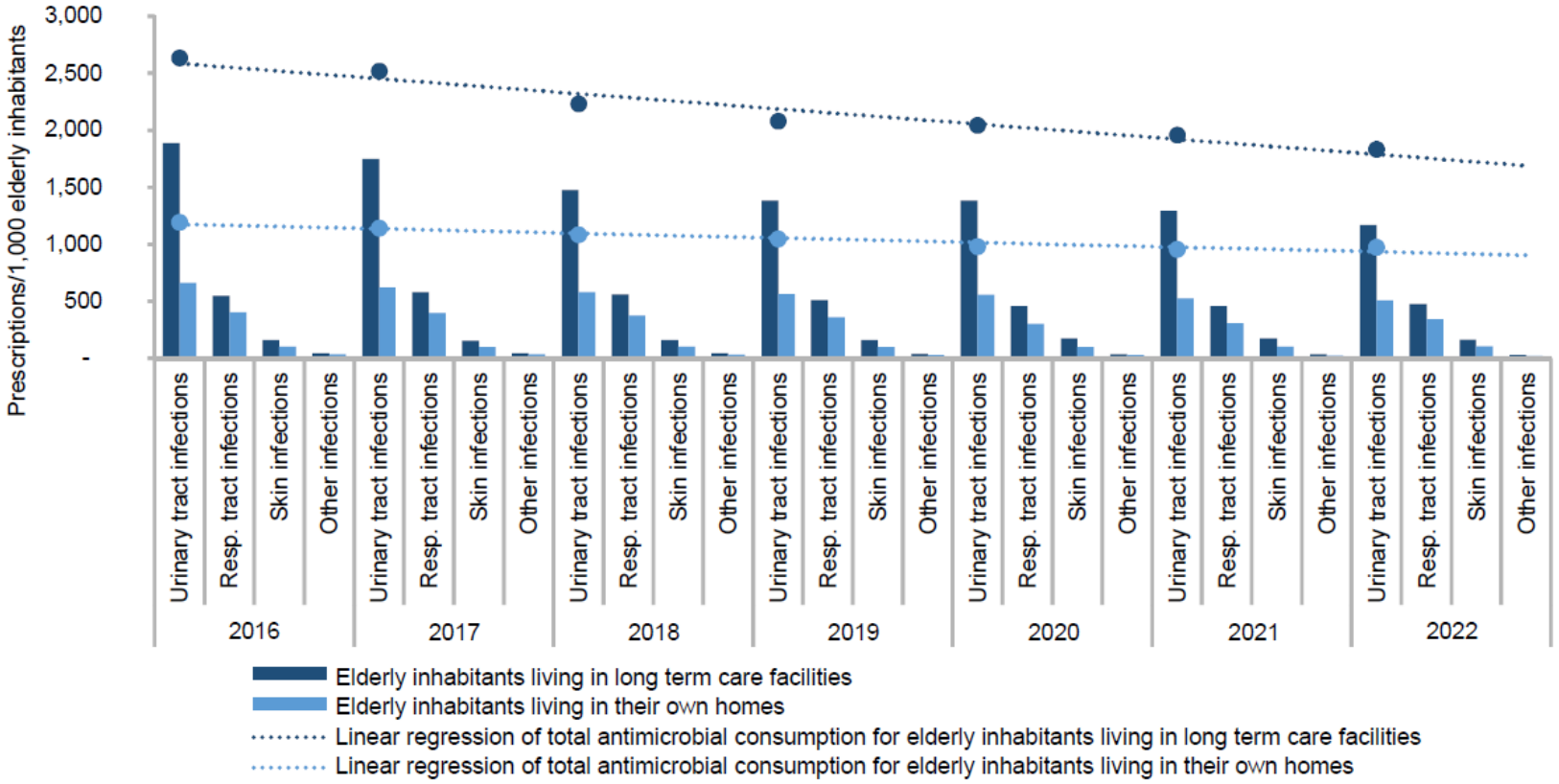


Antimicrobials in long term care facilities

Figure 5.14 Consumption of antimicrobials (J01 and P01AB01) in primary health care for elderly inhabitants living in long term care facilities and for elderly inhabitants living in their own homes, Denmark, 2016-2022 DANMAP 2022



Data: Registered sale of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics, 2023 edition of the Anatomical Therapeutic Chemical (ATC) classification system, Care Home Register and Danish Civil Registry

2016-2022 -30%

2016-2022 -18%

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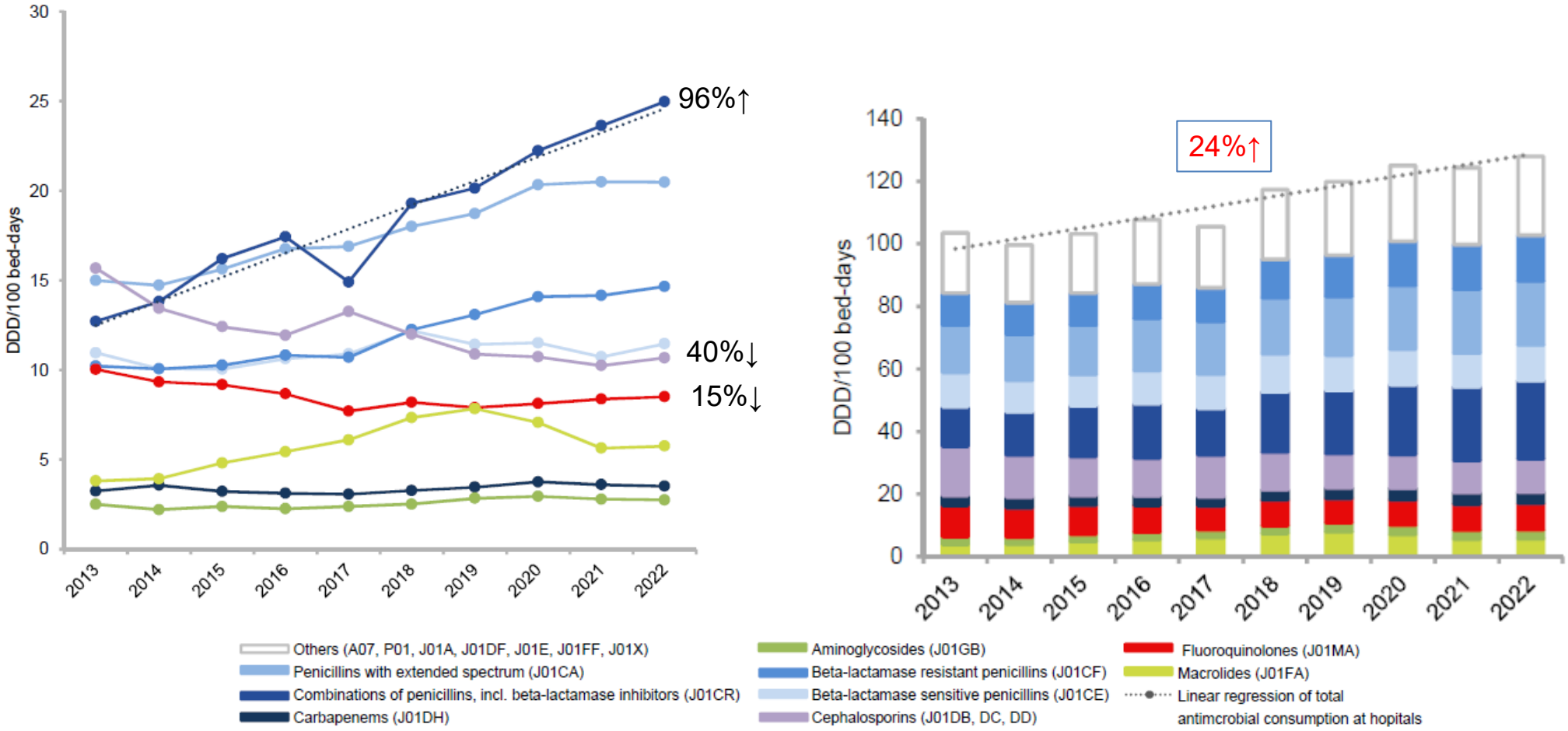
Antimicrobials in hospitals

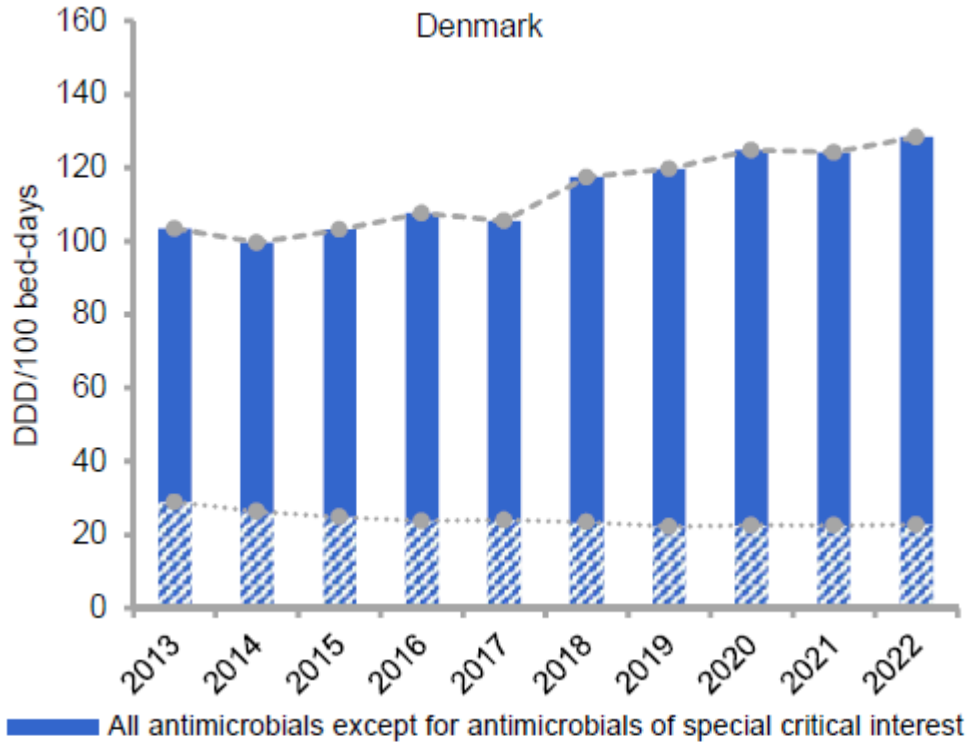
Figure 5.15 Consumption at somatic hospitals by leading groups of antimicrobial agents, DDD per 100 bed-days, Denmark, 2013-2022



Data: Antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics, 2023 edition of the Anatomical Therapeutic Chemical (ATC) classification system and The National Patient Register

Antimicrobials of special critical interest

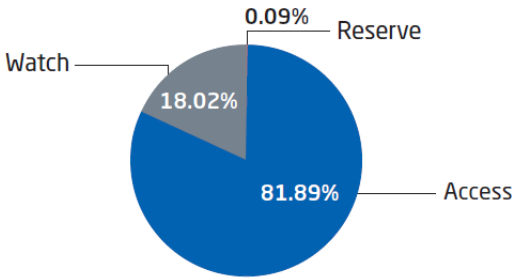
Figure 5.20 Consumption of antimicrobials of special critical interest (cephalosporins, fluoroquinolones and carbapenems) and all other antimicrobials in the five health regions, DDD per 100 bed-days, Denmark, 2013-2022 DANMAP 2022



AWaRe classification of antimicrobials in Denmark, 2022

The World Health Organization (WHO) has developed the AWaRe classification system as a tool to assist antibiotic stewardship and to reduce antimicrobial resistance. Antibiotics are classified into three groups to emphasize the importance of their appropriate use:

- **Access:** Antibiotics used to treat common susceptible pathogens with lower resistance potential than antibiotics in the other groups. 60% of total antimicrobial consumption should consist of Access agents.
- **Watch:** Antibiotics that have higher resistance potential and including most of the highest priority agents. These antibiotics should be prioritized as key targets of stewardship programs and monitoring.
- **Reserve:** Antibiotics reserved for treatment of confirmed or suspected infections due to multi-drug-resistant organisms. These antibiotics should be considered as "last resort" options.



WHO Access, Watch, Reserve (AWaRe) classification of antibiotics for evaluation and monitoring of use, 2021. Geneva: World Health Organization; 2021 (WHO/MHP/HPS/EML/2021.04)

World Health Organization

Data: Antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics, 2023 edition of the Anatomical Therapeutic Chemical (ATC) classification system and The National Patient Register

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International surveillance of antimicrobials

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Take-home message

- Consumption of antimicrobials in Denmark has decreased in the last 10 years, but the consumption is bouncing back to the pre-pandemic level
- Consumption of antimicrobials in primary health care follows waves of various respiratory infections
- Elderly inhabitants aged 65 and above living in long term care facilities received 88% more antibiotics in 2022 than elderly inhabitants living in their own homes, despite consumption for in long term care facilities decreased by 30% from 2016 to 2022
- Consumption of broad-spectrum antimicrobials in hospitals continues to rise and is compensated by dispensing permits in case of shortages
- Consumption of antimicrobials of special critical interest in hospitals continues to decrease.

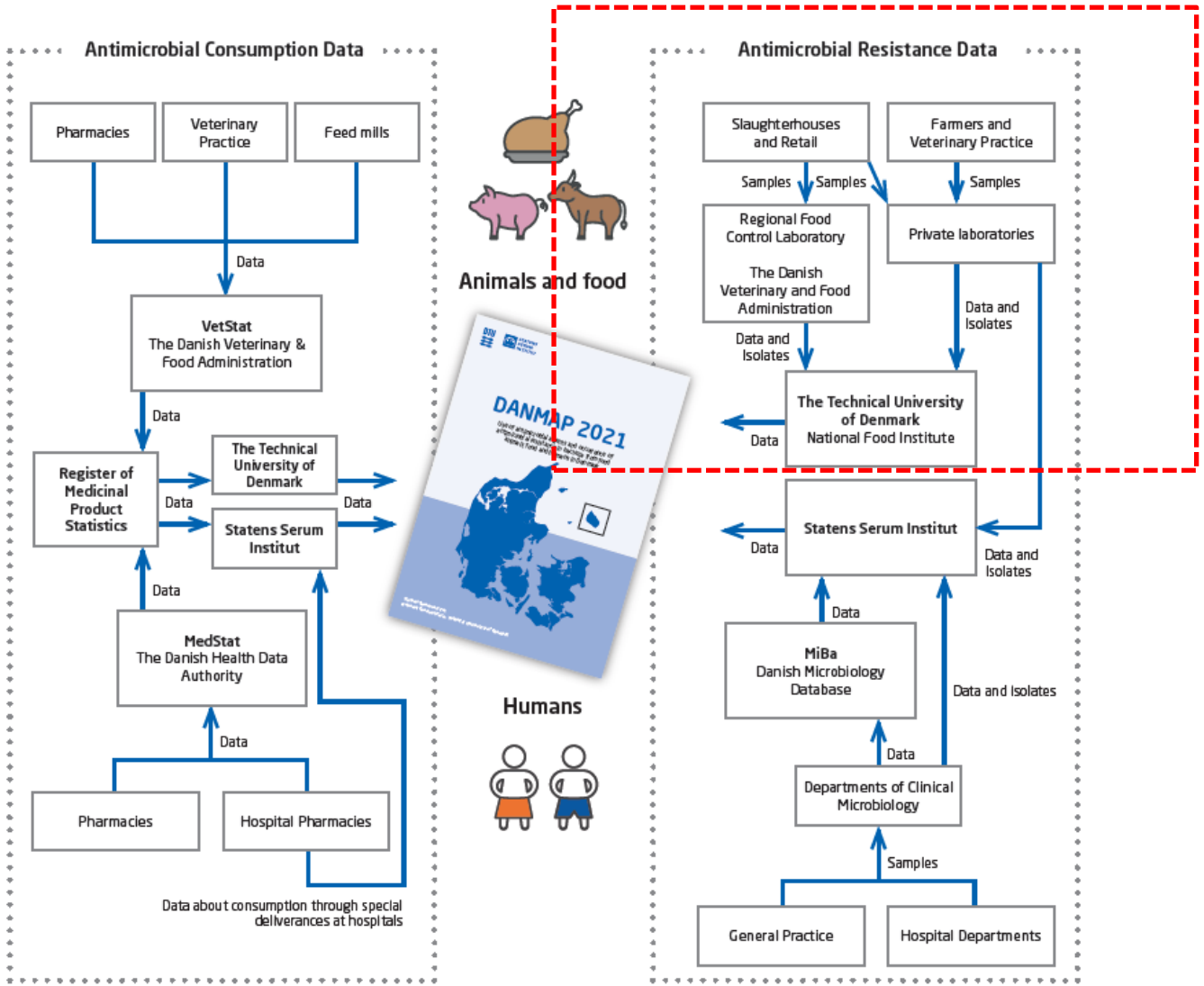
Thank you for your attention!

- Find us here www.danmap.org

Antimicrobial resistance in bacteria from food animals and food

Ana Sofia Ribeiro Duarte
Senior Researcher, DVM, PhD

Foodborne Pathogens and Epidemiology
DTU National Food Institute


Antimicrobial Consumption Data
Pharmacies
Veterinary Practice
Feed mills
Data
VetStat
The Danish Veterinary & Food Administration
Data
Register of Medicinal Product Statistics
Data
The Technical University of Denmark
Statens Serum Institut
Data
Data
MedStat
The Danish Health Data Authority
Data
Pharmacies
Hospital Pharmacies
Data about consumption through special deliverances at hospitals
Animals and food
DANMAP 2021
Humans
Antimicrobial Resistance Data
Slaughterhouses and Retail
Farmers and Veterinary Practice
Samples
Samples
Samples
Regional Food Control Laboratory
The Danish Veterinary and Food Administration
Private laboratories
Data and Isolates
Data and Isolates
Data
The Technical University of Denmark
National Food Institute
Data
Statens Serum Institut
Data and Isolates
Data
MiBa
Danish Microbiology Database
Data and Isolates
Data
Departments of Clinical Microbiology
Samples
General Practice
Hospital Departments

EU legislation for harmonized AMR monitoring

Decision 2020/1729/EU, 1 January 2021:

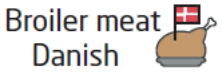
- Mandatory monitoring of:
  - *Campylobacter coli*
  - ESBL-, AmpC- or CP-producing *E. coli* in fresh turkey meat sampled at retail and at BCPs **(even years)**

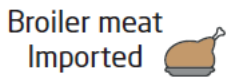
Overview of animal isolates reported in DANMAP 2022

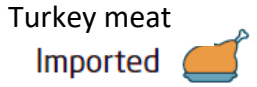
Caecal samples:

- All samples: indicator *E. coli*
- Broilers and cattle: *Campylobacter spp. (C. jejuni, C. coli,* other species*)*
- Broilers: ESBL/AmpC/CP-producing *E. coli* and *Enterococcus spp. (E. faecium, E. faecalis)*

Meat samples collected at retail:







- Broiler meat and turkey meat: ESBL/AmpC/carbapenemase-producing *E. coli*
- Imported pork: *Salmonella spp.*

Carcass swabs at the slaughterhouse:

- Pig carcasses: *Salmonella spp.* (national control program)

Ana Sofia R. Duarte (DTU Food)
Jeppe Boel (SSI)

Resistance in zoonotic bacteria - Textboxes

Textbox 6.1 – Detection of resistance genes and point mutations in *Salmonella* and *Campylobacter* using whole genome sequencing

Jeppe Boel (SSI)

Figure 1 Prevalence of resistance genes and/or point mutations conferring resistance to selected antimicrobial classes in 649 clinical human isolates of *C. jejuni* and in 58 isolates of *C. coli*, Denmark, 2022 DANMAP 2022

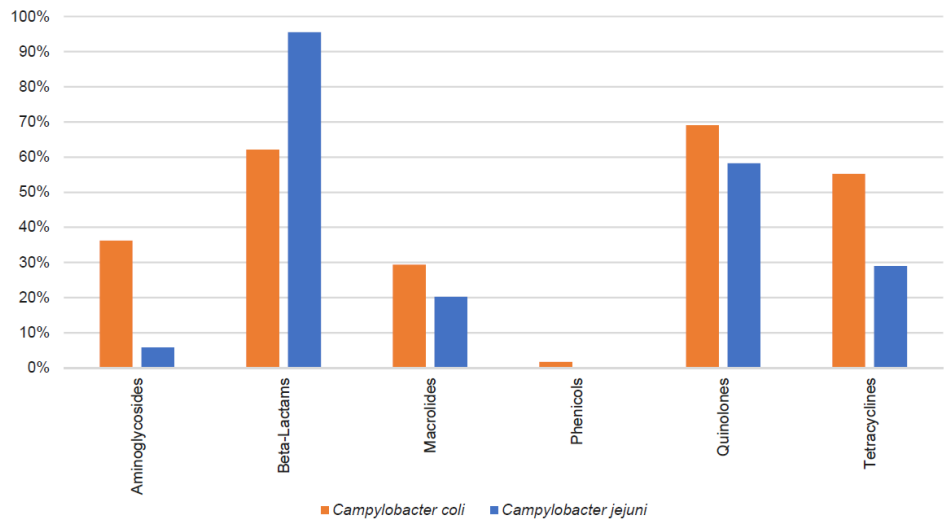
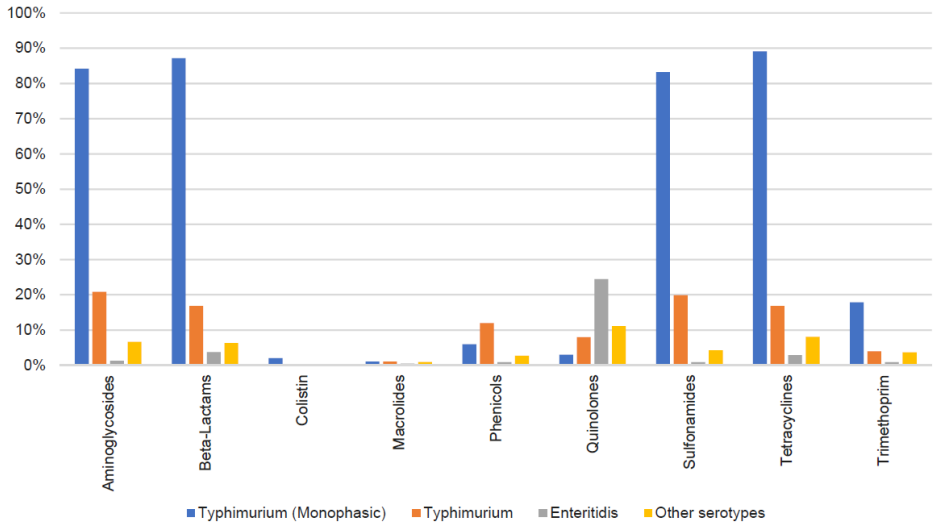
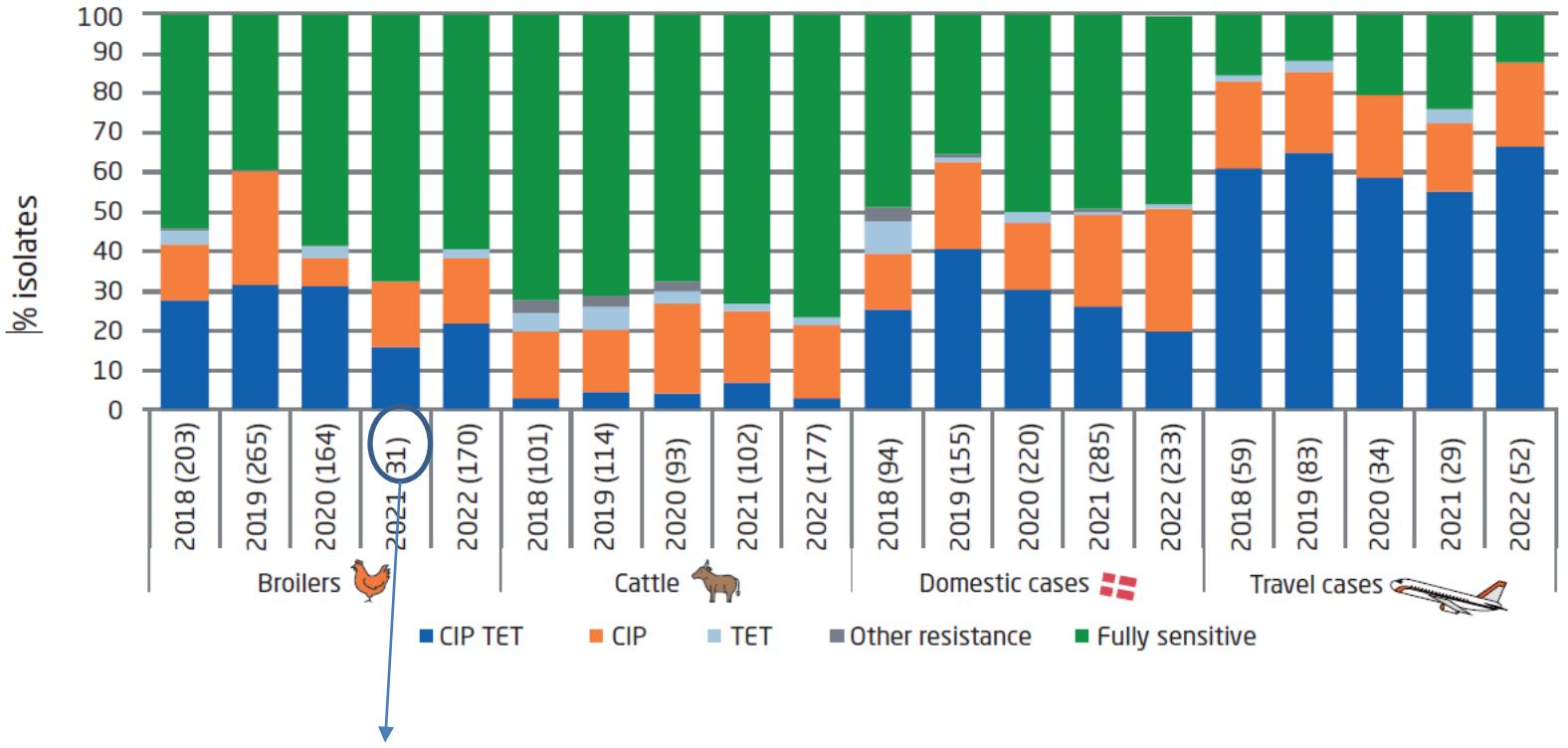


Figure 2 Prevalence of resistance genes and/or point mutation conferring resistance to selected antimicrobial classes in 782 clinical human isolates of *Salmonella*, Denmark, 2022 DANMAP 2022



DANMAP 2022– *Campylobacter jejuni*

Figure 4.1 Distribution (%) of AMR profiles among *Campylobacter jejuni* from broilers, cattle and human cases, Denmark, 2018-2022



few isolates in 2021!

- Increase in **%FS** from last 2 years in **broilers** discontinued in 2022
- **%FS** isolates in **cattle** continued to increase
- **% CIP/TET** on decreasing trend and **%CIP** on increasing trend among **domestic cases**
- Resistance overall highest among **travel cases**, and lower **%FS** in 2022

DANMAP 2022– *C. jejuni and C. coli*

Table 4.1 Resistance (%) in *Campylobacter jejuni* isolates from broilers, cattle and human cases, Denmark, 2022

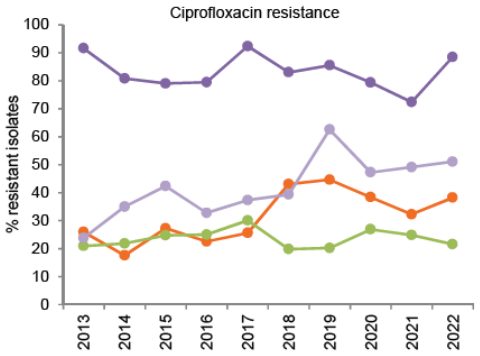
	Broilers	Cattle	Human		
	Danish	Danish	Domestically acquired	Travel abroad reported	Total
Antimicrobial agent	%	%	%	%	%
Chloramphenicol	0	0	0	0	0
Ciprofloxacin	38	22	51	88	58
Ertapenem	2	0	1	12	3
Erythromycin	0	0	0	0	0
Gentamicin	0	0	0	0	0
Tetracycline	24	5	21	67	29
Fully sensitive (%)	59	76	48	12	41
Number of isolates	170	102	233	52	285

- Higher AMR occurrence in **human** isolates
- Common **CIP** and **TET** resistance
- **Ertapenem** resistance detected in *C. jejuni* from broilers and humans (highest among travel cases)
- **CIP** on increasing trend

***Campylobacter coli*:**

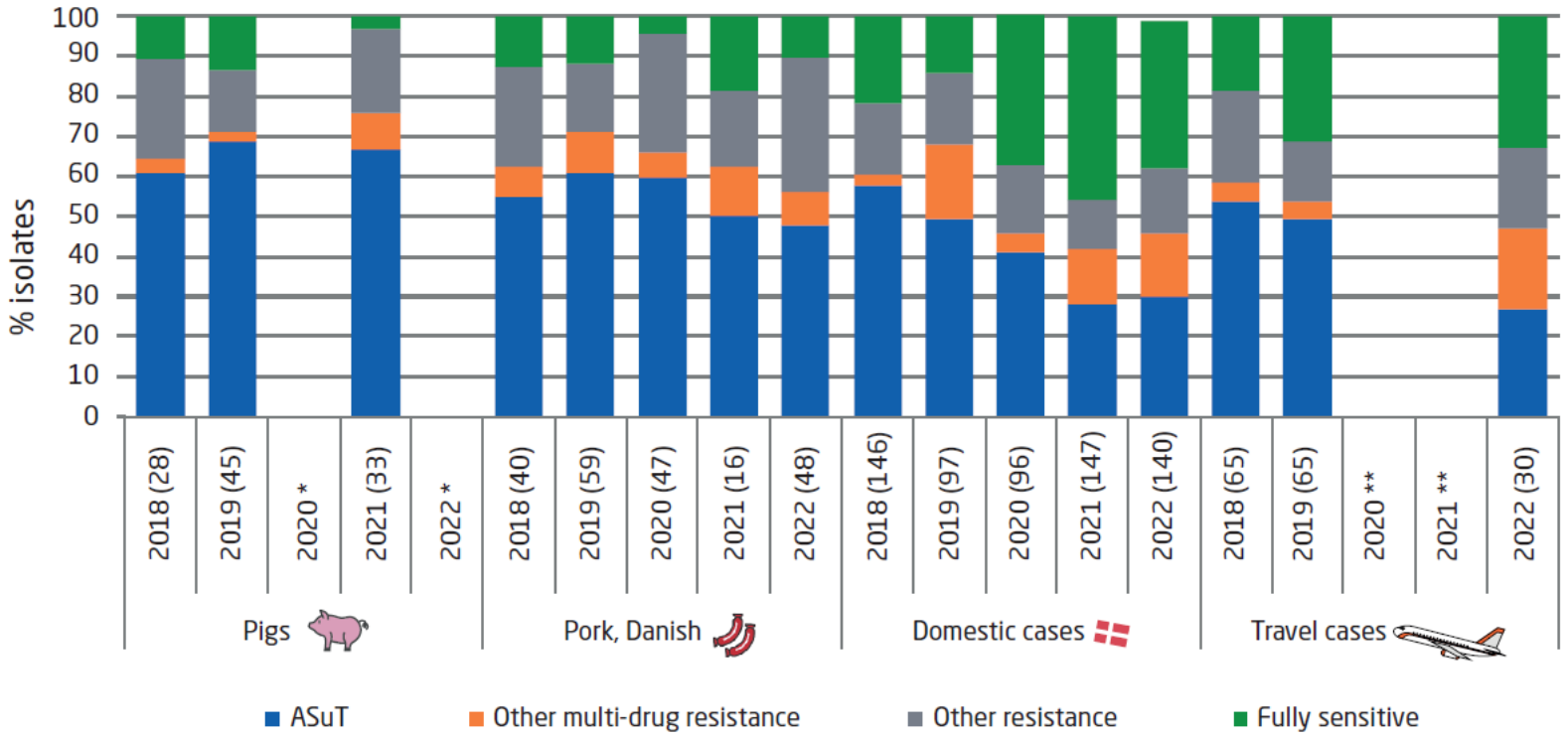
- Ciprofloxacin resistance similar to *C. jejuni* (39%)
- Tetracycline resistance higher in *C. coli* (45%)
- Gentamicin, erythromycin and chloramphenicol resistance - not observed
- Ertapenem resistance markedly higher in *C. coli* (23%)

Broilers



DANMAP 2022 – *Salmonella* Typhimurium

Figure 4.2 Distribution (%) of AMR profiles among *Salmonella* Typhimurium from pigs, pork and human cases, Denmark, 2018-2022



- **ASuT** remains most common MDR profile, but on decreasing trend
- **%FS** isolates from pork and domestic cases decreased
- Majority of **ASuT** isolates from **humans** were monophasic ST34

DANMAP 2022– *Salmonella* Typhimurium

Table 4.2 Resistance (%) in *Salmonella* Typhimurium isolates from domestic pork and humans, Denmark, 2022

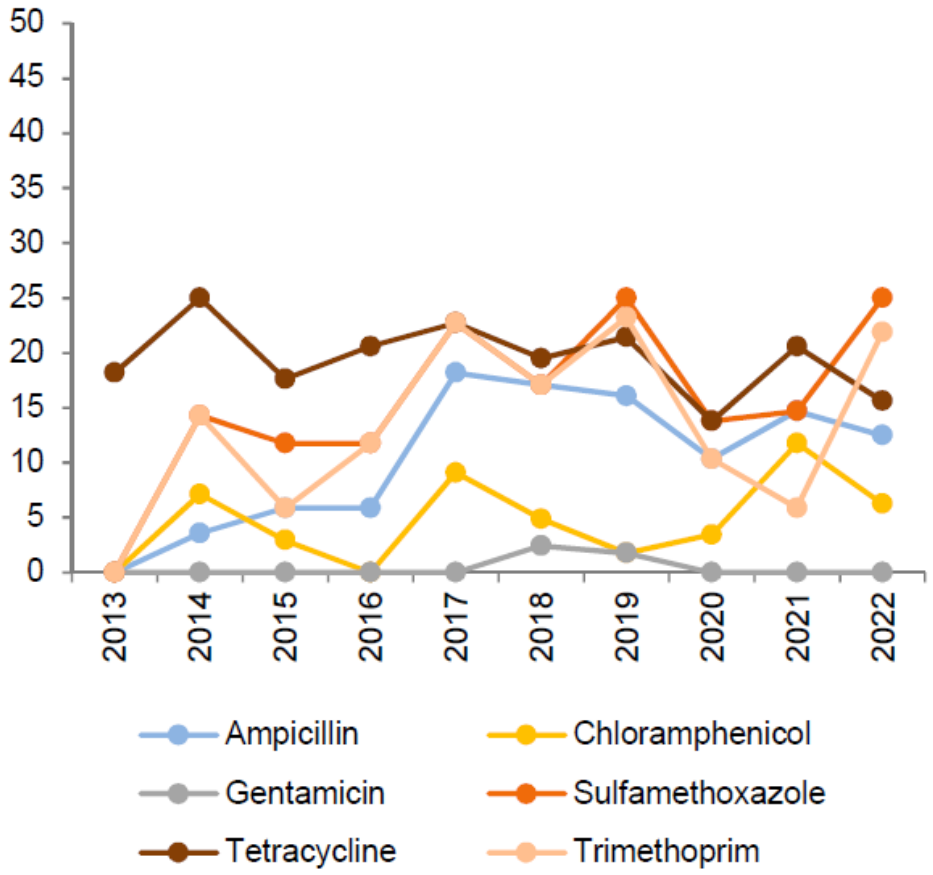
	Pork	Human					
	Danish	Domestically acquired	Travel abroad reported	Unknown origin	Total	*S.* Typhimurium diphasic	*S.* Typhimurium monophasic
Antimicrobial agent	%	%	%	%	%	%	%
Amikacin	0	2	7	0	3	1	4
Ampicillin	79	51	53	35	50	15	86
Azithromycin	4	0	3	0	1	1	0
Cefotaxime	0	1	3	0	1	0	2
Ceftazidime	0	1	3	0	1	0	2
Chloramphenicol	13	6	13	5	7	10	4
Ciprofloxacin	0	4	20	0	6	8	3
Colistin	0	1	7	0	2	2	1
Gentamicin	8	1	3	0	1	0	2
Meropenem	0	0	0	0	0	0	0
Nalidixic acid	0	4	13	0	5	6	3
Sulfamethoxazole	81	54	47	35	51	19	84
Tetracycline	56	55	50	25	51	15	88
Tigecycline	2	1	0	0	1	2	0
Trimethoprim	25	11	7	5	9	4	15
Fully sensitive (%)	10	37	33	65	39	74	4
Number of isolates	48	140	30	20	190	96	94

- Absent or rare resistance to **3rd generation cephalosporins**, **meropenem**, **colistin**, **amikacin**, and **tigecycline**

- Higher AMR occurrence in **pork** isolates
- **Azithromycin** resistance detected at low levels in **pork** isolates and in **travel cases**
- **Fluoroquinolone** (ciprofloxacin and nalidixic acid) resistance detected in **human** isolates, mostly in travel cases

DANMAP 2022– *Salmonella* Derby

Figure 6.5 Resistance (%) among *Salmonella* Derby from domestic pork, Denmark DANMAP 2022



- Lower AMR occurrence than S. Typhimurium (69% **FS**)
- Increase in occurrence of resistance to **sulfamethoxazol** and **trimethoprim** resistance
- Decrease in resistance to **ampicillin, tetracycline** and **chloramphenicol.**
- Low or absent resistance to azithromycin, tigecycline, amikacin, 3rd and 4th generation cephalosporins, colistin, gentamicin, meropenem or fluoroquinolones.

Ana Sofia R. Duarte (DTU Food)

Resistance in indicator bacteria - Textboxes

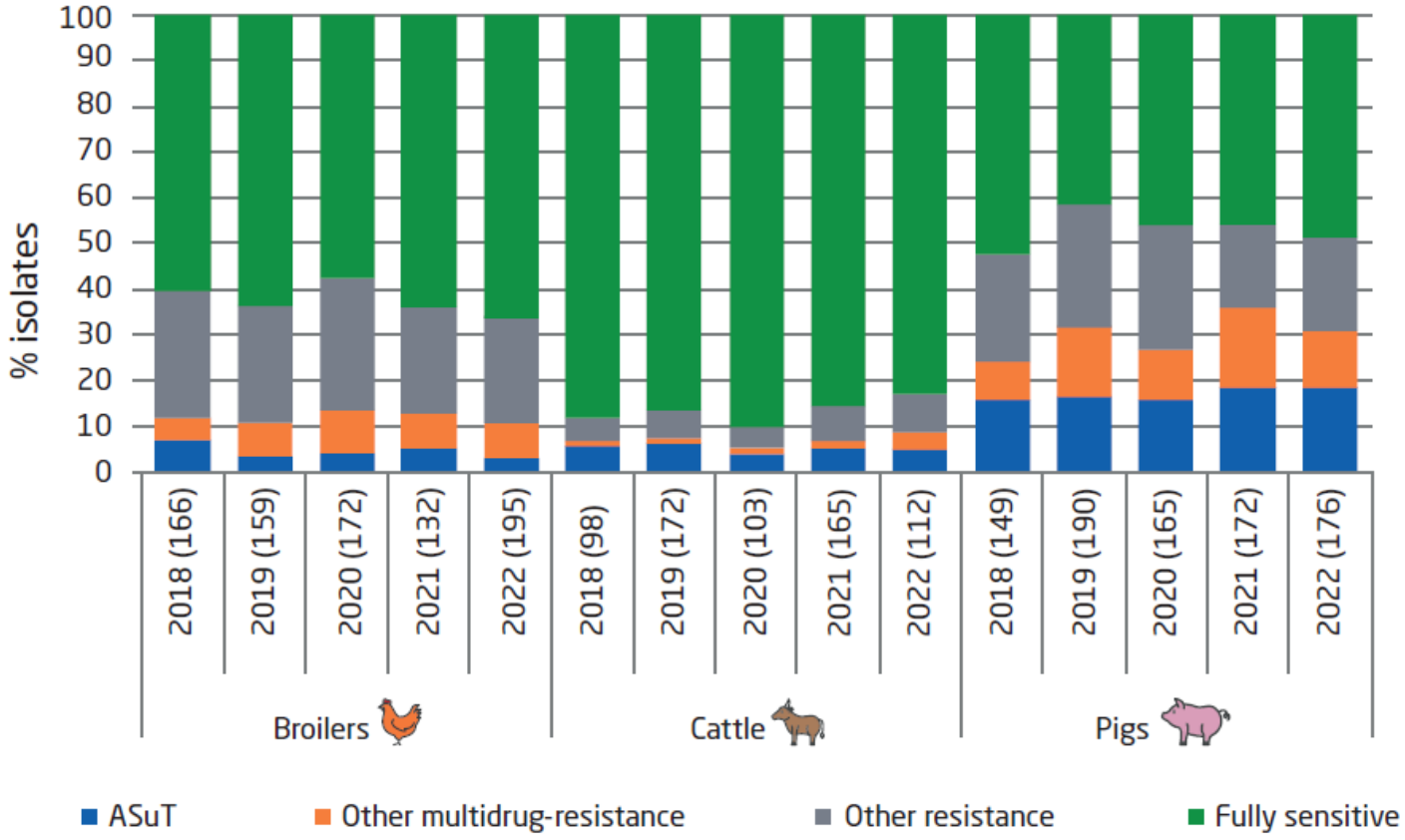
Textbox 7.1 – Antimicrobial resistance trends in indicator *E. coli* in Danish pigs, broilers, and cattle 2014 to 2022

Joana Pessoa (DTU Food)

Figure 1 Monthly proportion of fully sensitive and multidrug-resistant indicator *E. coli* isolated from broilers (n = 1,411), Denmark 2014-2022. The grey lines identify the time series trend calculated using the locally weighted regression (LOESS) method DANMAP 2022

DANMAP 2022 - Indicator *E. coli*

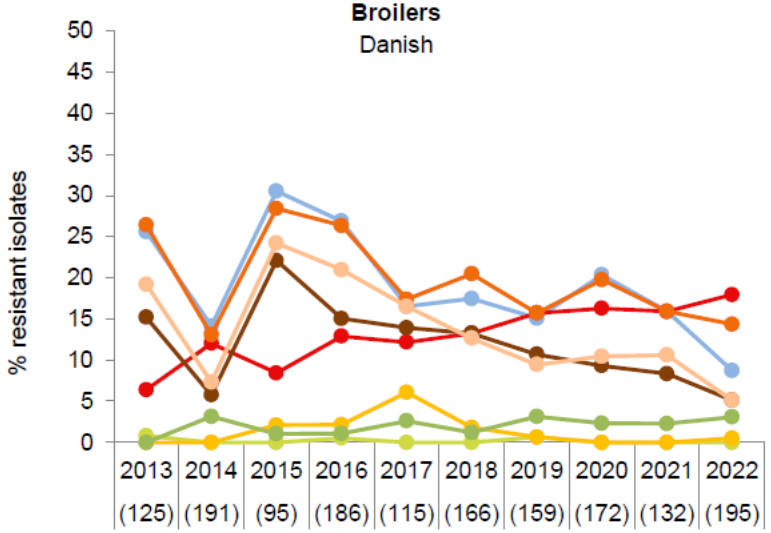
Figure 5.1 Distribution (%) of fully-sensitive, resistant and multidrug-resistant *Escherichia coli* isolates from broilers, cattle and pigs, Denmark, 2018-2022



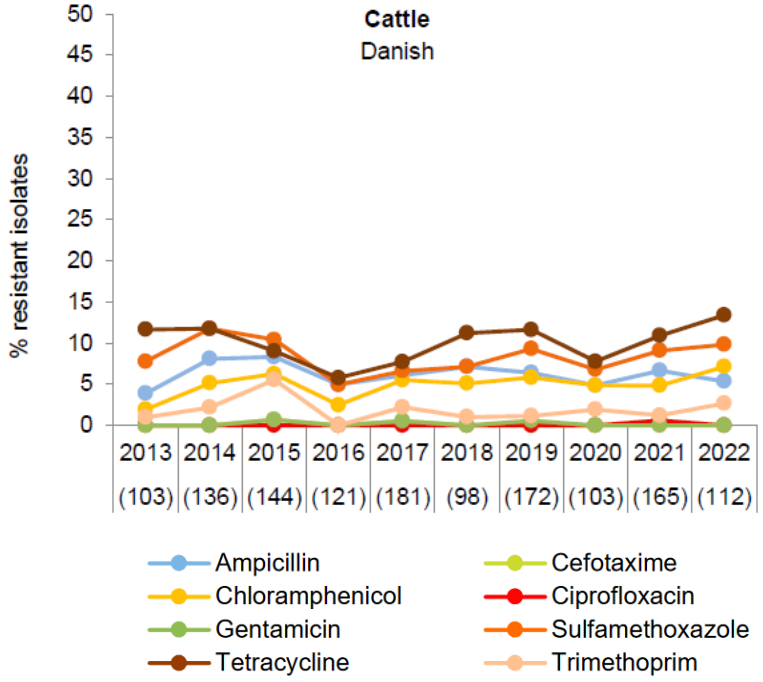
- **%FS** isolates continued to increase in **broilers** and to decrease in **cattle**, however
- No significant trend in **%FS** in the last 5 years
- **%MDR** isolates decreased in **pigs** and **broilers** and increased in **cattle**

DANMAP 2022 - Indicator *E. coli*

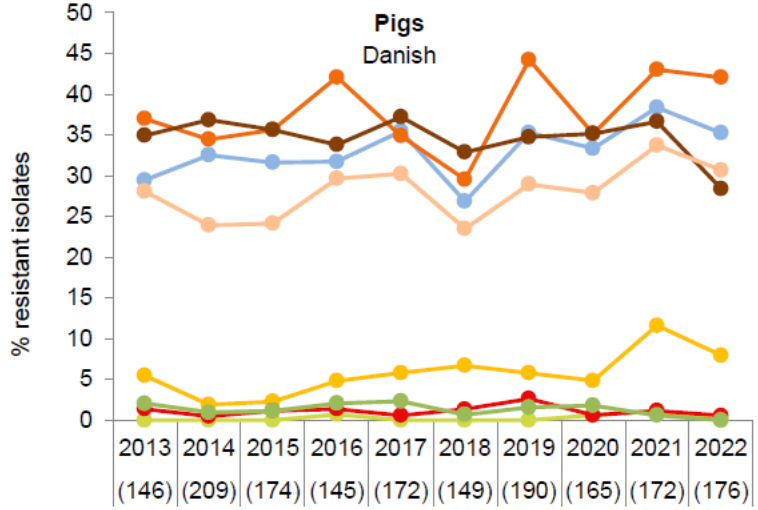
Broilers



Cattle



Pigs



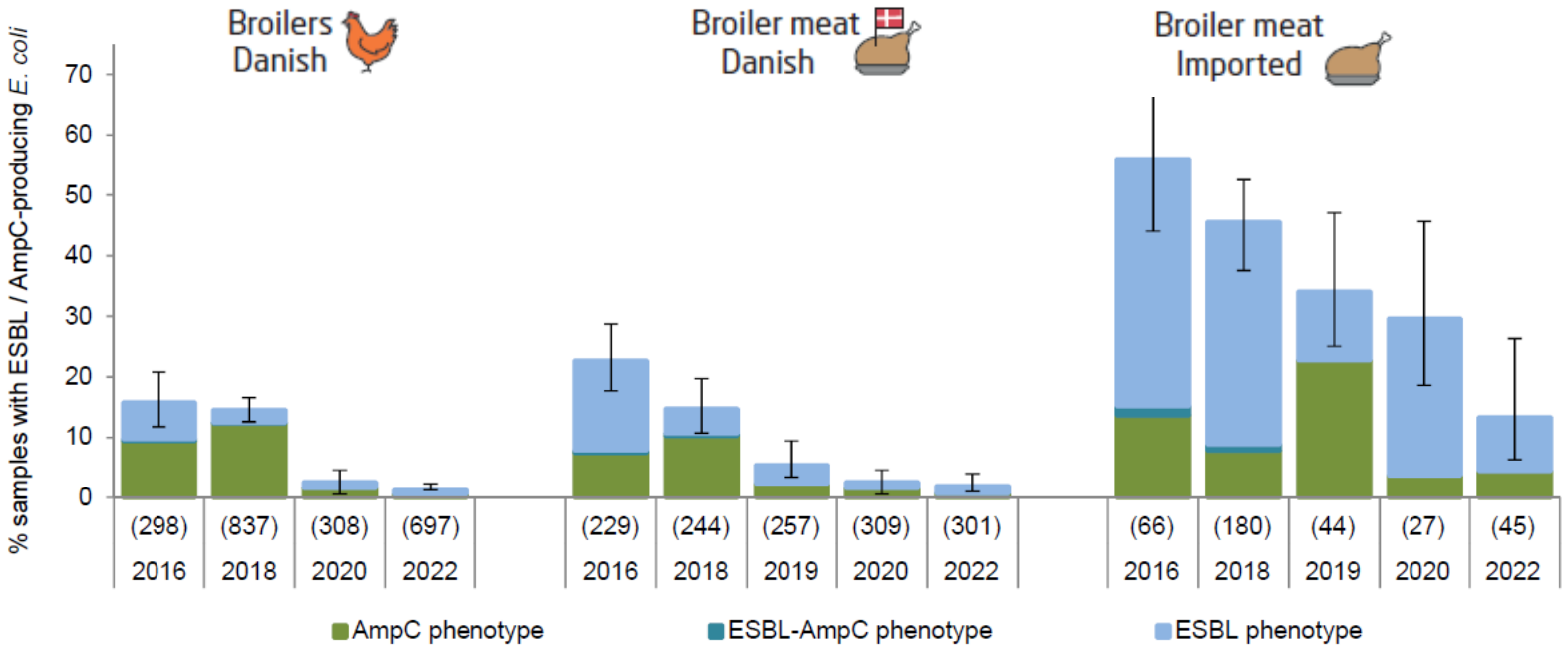
- Increase in **ciprofloxacin** resistance in **broiler** isolates
- Increase in % resistance to several substances in isolates from **cattle**

- Decrease in % resistance to most substances in isolates from **pigs**
- Decrease in % resistance to **ASuT** substances in isolates from **broilers**

DANMAP 2022 - ESBL-, AmpC-, CP-producing *E. coli*

Figure 7.3 Occurrence (%) of samples with phenotypic ESBL- or AmpC-producing *E. coli* from animals and meat recovered by selective enrichment, Denmark 2016-2022

DANMAP 2022



- %ESBL- or AmpC-producing *E. coli* continued to decrease in **broilers** and **broiler meat**
- %ESBL- or AmpC-producing *E. coli* still higher in **imported broiler meat**
- No detection of CP-producing *E. coli*

Turkey meat Imported

- 52% of **imported turkey meat** samples presented ESBL- and/or AmpC-producing *E. coli*

DANMAP 2022 - ESBL-, AmpC- producing *E. coli*

Table 5.2 Number of ESBL and/or AmpC enzymes detected in β-lactamase-producing *E. coli* isolates from animals and meat recovered by selective enrichment, Denmark, 2022

	Broilers	Broiler meat		Turkey meat
	Danish	Danish	Import	Import
CTX-M-1	2	1		3
CTX-M-14				2
CTX-M-15				28
CTX-M-27				6
CTX-M-32				2
CTX-M-55			2	5
CTX-M-65			1	1
OXA-1				2
SHV-12		1		6
TEM-135				3
TEM-176				1
TEM-1B	3	1	4	21
TEM-1D				1
TEM-52B	1	2		
CMY-2	1	1	2	
Chromossomal AmpC (C-42T)	3	1		3
Number of AmpC genotypes	1	1	1	3
Number of ESBL genotypes (two or more enzymes)	3 (0)	4 (0)	4 (2)	54 (25*)
Number of AmpC+ESBL genotypes	3	1	1	0
Not available	2	0	0	2
Number (%) positive samples	9 (1%)	6 (2%)	6 (13%)	59 (52%)
Number of tested samples	697	307	45	113
Number of AmpC phenotypes	4	2	2	3
Number of ESBL phenotypes	5	4	4	53
Number of ESBL+AmpC phenotypes	0	0	0	3

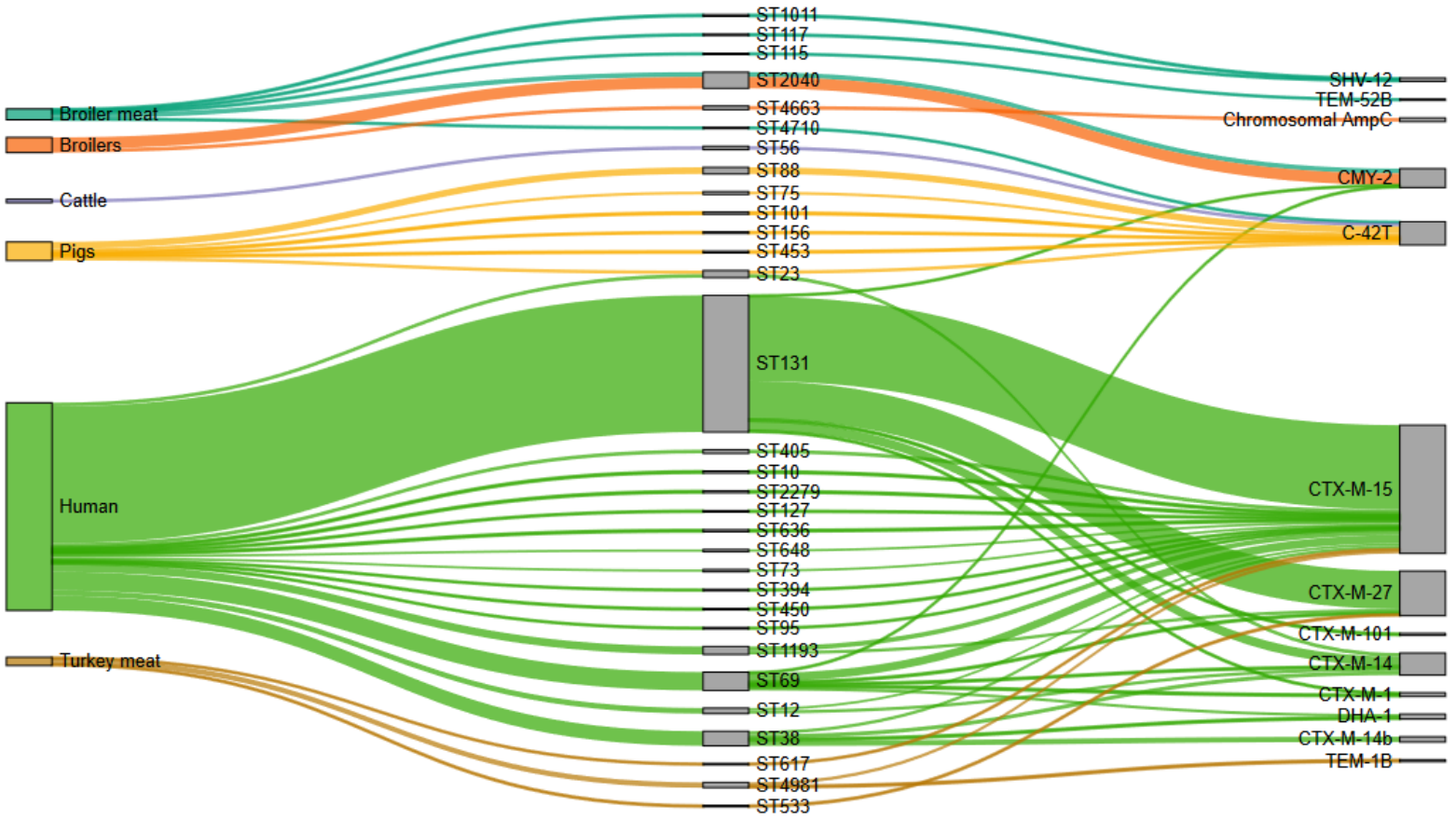
- Phenotypic and genotypic profiles mostly in concordance
- 14 different **ESBL genes** detected, 9 as the only encoding gene
- Genes **CTX-M-1** and **TEM-1B** most common among ESBL-producing isolates
- **CTX-M-15** highly frequent in isolates from **imported turkey meat**
- 46% of isolates from **turkey meat** with more than one ESBL encoding gene
- Upregulated AmpC promotor **C-42T** mutations most common among AmpC-producing isolates
- All **AmpC+ESBL-producing** isolates with gene **TEM-1B**

DANMAP 2022 - ESBL-, AmpC- producing *E. coli*

Table 5.2 Number of ESBL and/or
meat recovered by selective enri

CTX-M-1
CTX-M-14
CTX-M-15
CTX-M-27
CTX-M-32
CTX-M-55
CTX-M-65
OXA-1
SHV-12
TEM-135
TEM-176
TEM-1B
TEM-1D
TEM-52B
CMY-2
Chromossomal AmpC (C-42T)
Number of AmpC genotypes
Number of ESBL genotypes (two or m
Number of AmpC+ESBL genotypes
Not available
Number (%) positive samples
Number of tested samples
Number of AmpC phenotypes
Number of ESBL phenotypes
Number of ESBL+AmpC phenotypes

Figure 8.1 A Sankey diagram showing the source, MLST and ESBL/AmpC gene of the included isolates. Flows of a minimum of five are shown



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DANMAP 2022 - Indicator *Enterococcus faecalis*

Figure 7.4 Resistance (%) among Enterococci isolates from broilers, Denmark 2012-2022 DANMAP 2022

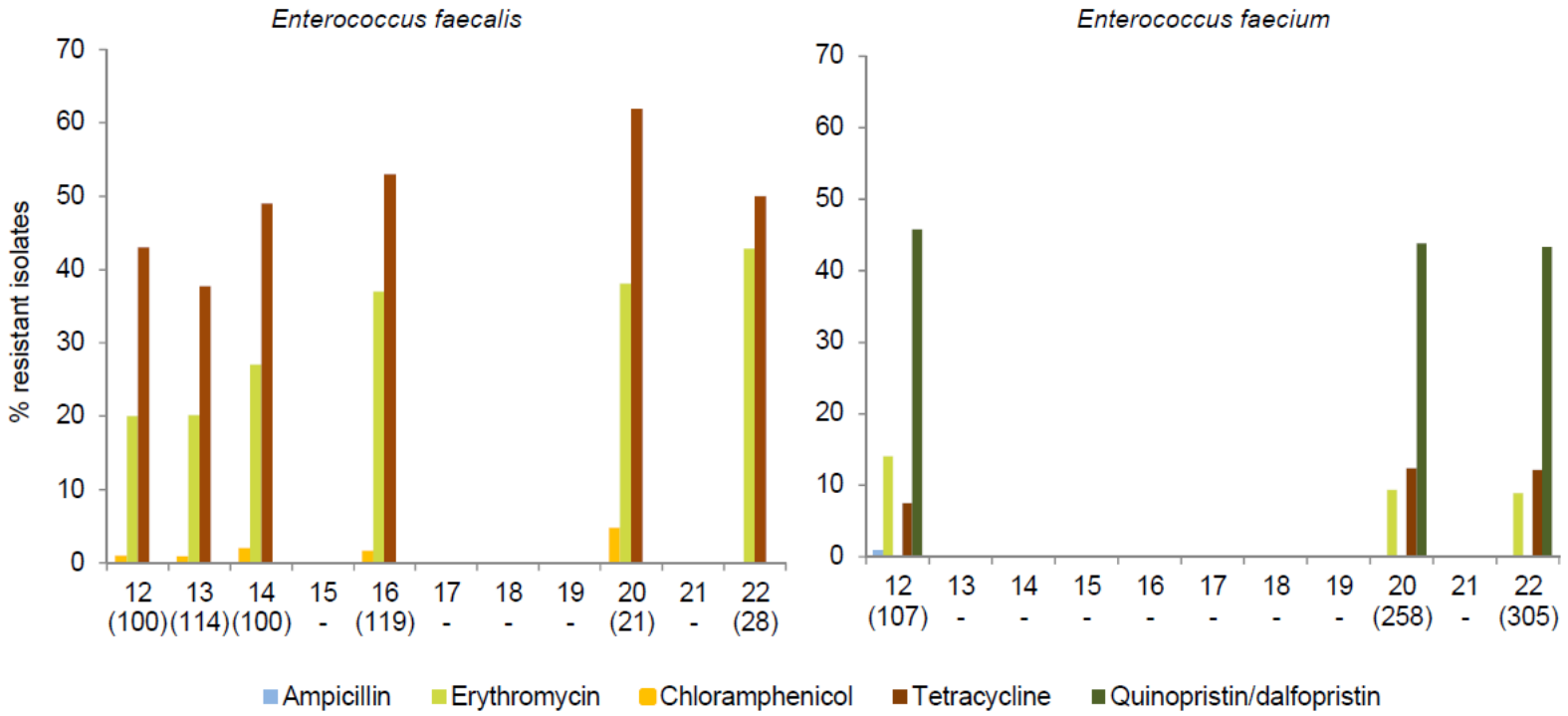
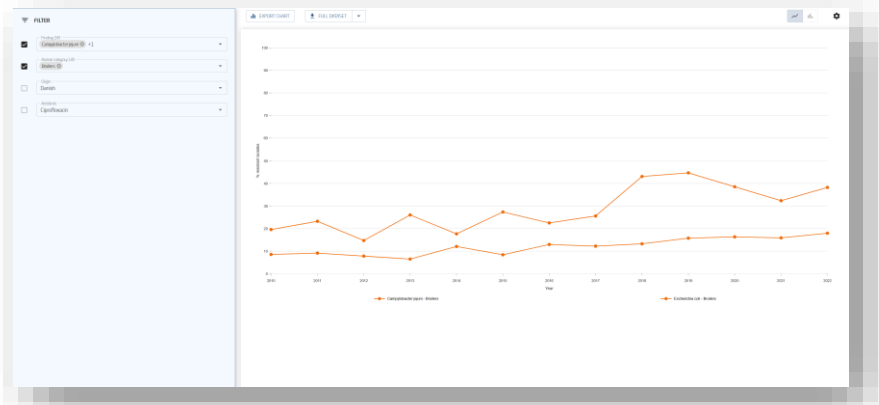


Table 7.4 Resistance (%) in Enterococci isolates from broilers, Denmark DANMAP 2022

Antimicrobial agent	*Enterococcus faecalis* %	*Enterococcus faecium* %
Ampicillin	0	0
Chloramphenicol	0	0
Ciprofloxacin	0	3
Daptomycin	0	0
Erythromycin	43	9
Gentamicin	0	0
Linezolid	0	0
Quinupristin/dalfopristin	-	43
Teicoplanin	0	0
Tetracycline	50	12
Tigecycline	0	0
Vancomycin	0	0
Fully sensitive (%)	39	52
Number of isolates	28	305

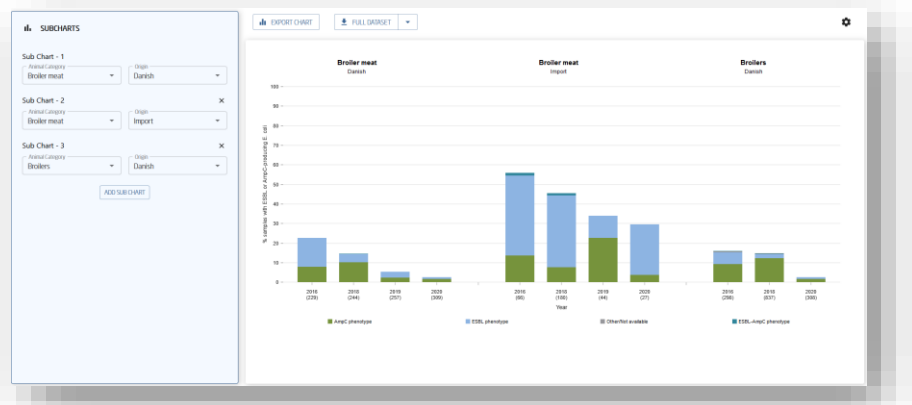
- ***E. faecium*** with levels of % resistance similar to 2020
- ***E. faecalis*****:** decrease in % **tetracycline** resistance and increase in % **erythromycin** resistance compared to 2020

DANMAP Explorer - interactive AMR data visualisation



DANMAP Explorer 1

Explore data on resistance in indicator and zoonotic bacteria



DANMAP Explorer 2

Explore data on ESBL/AmpC-producing *E. coli*

Available at : www.danmap.org

Resistance in human pathogens

Danish Programme for surveillance of antimicrobial consumption and resistance in bacteria from food animals, food and humans

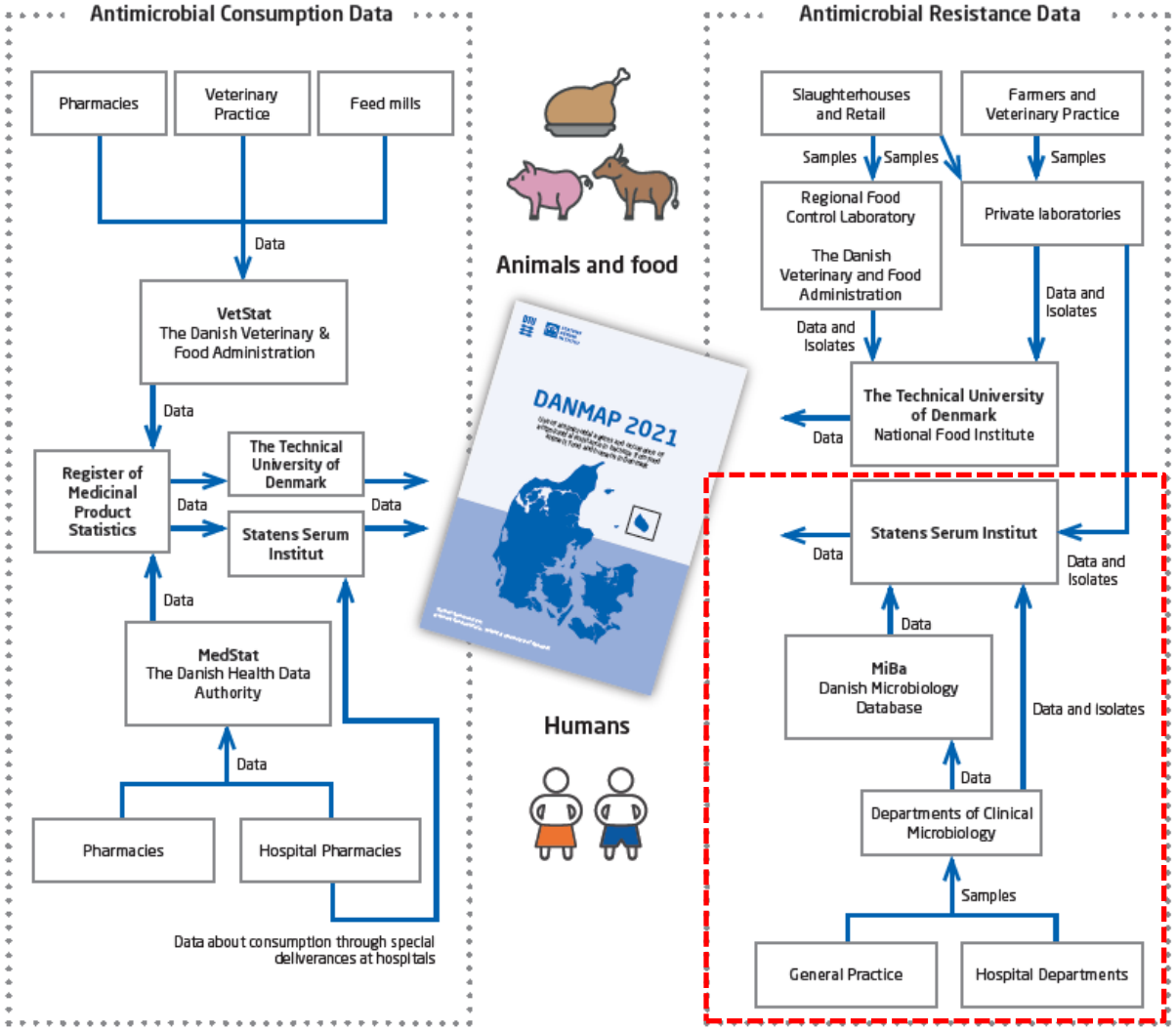
Mikkel Lindegaard
MSc Eng (biotech), PhD

National Reference Laboratory for Antimicrobial Resistance
Statens Serum Institut

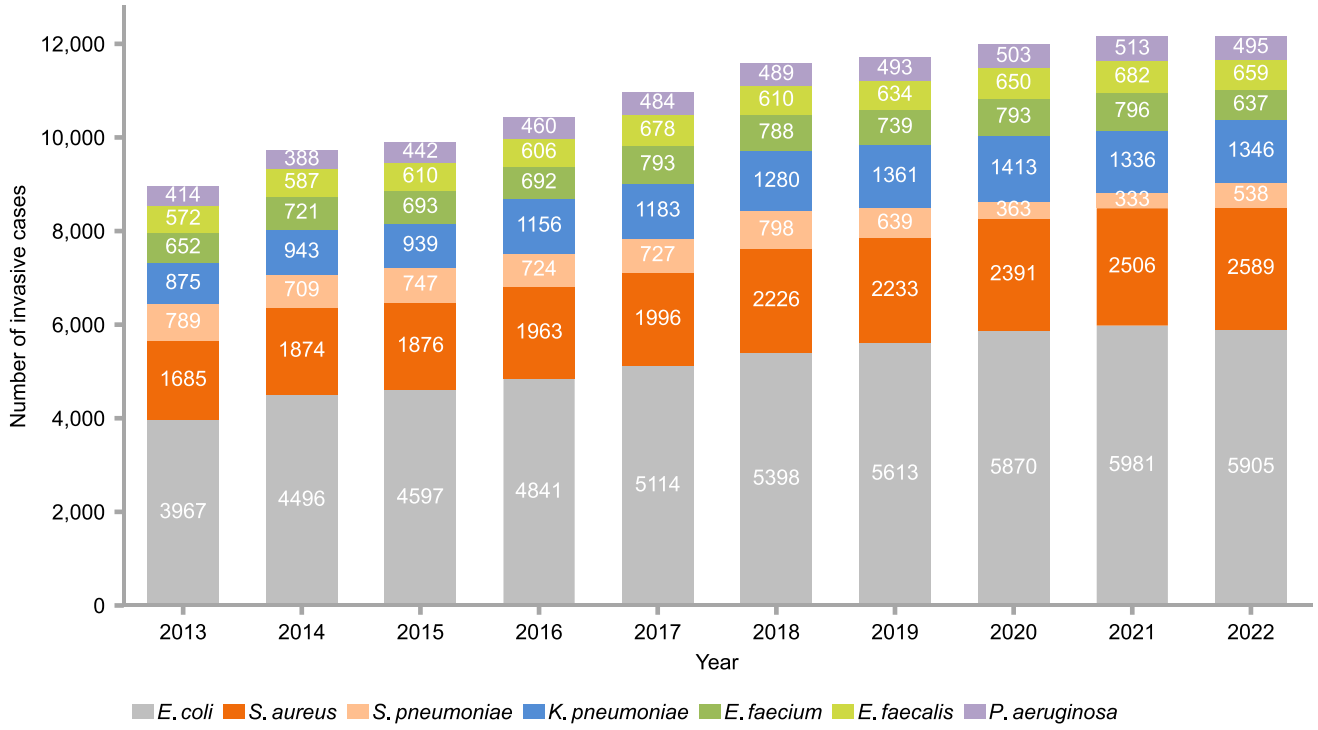
This year’s textboxes

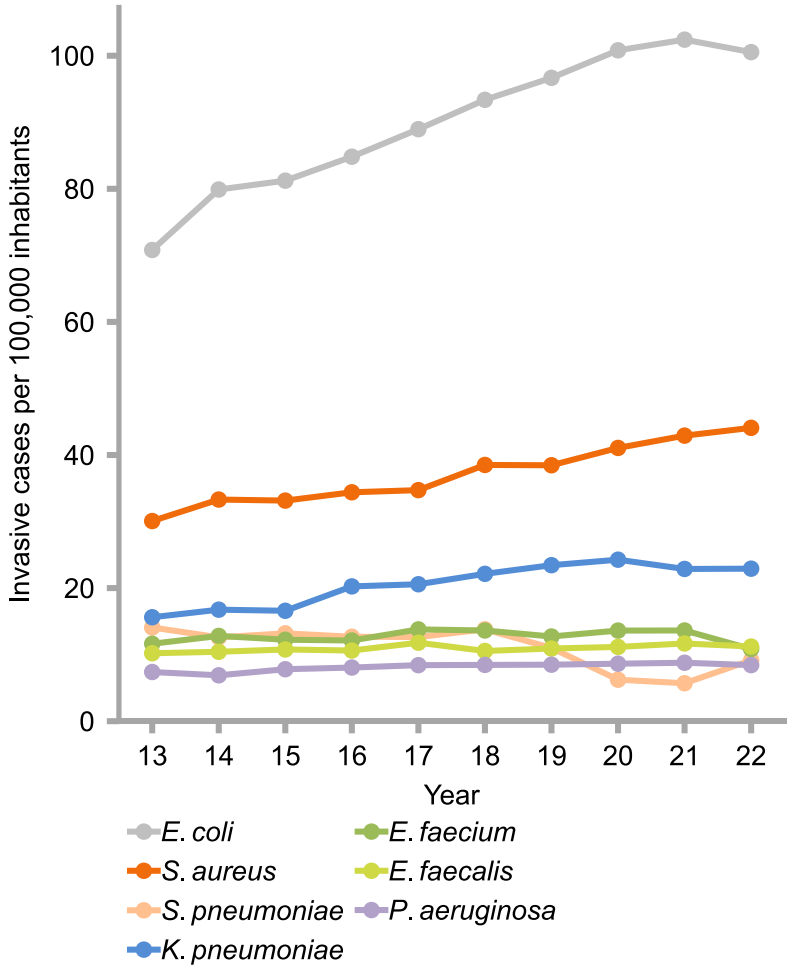
- Textbox 8.1 - Dicloxacillin capsules contaminated with CPE in Denmark and Iceland
- Textbox 8.2 - Fungaemia epidemiology, resistance rates and human antifungal consumption: a 2021-2022 update
- Textbox 8.3 - *Mycoplasma genitalium*

Resistance in human pathogens

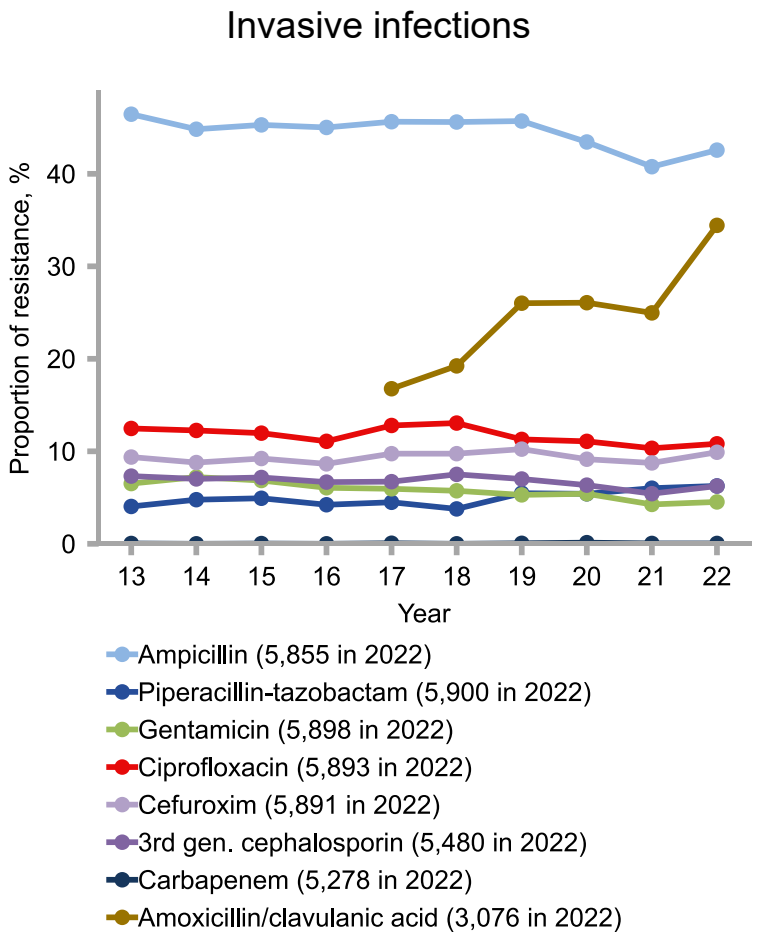


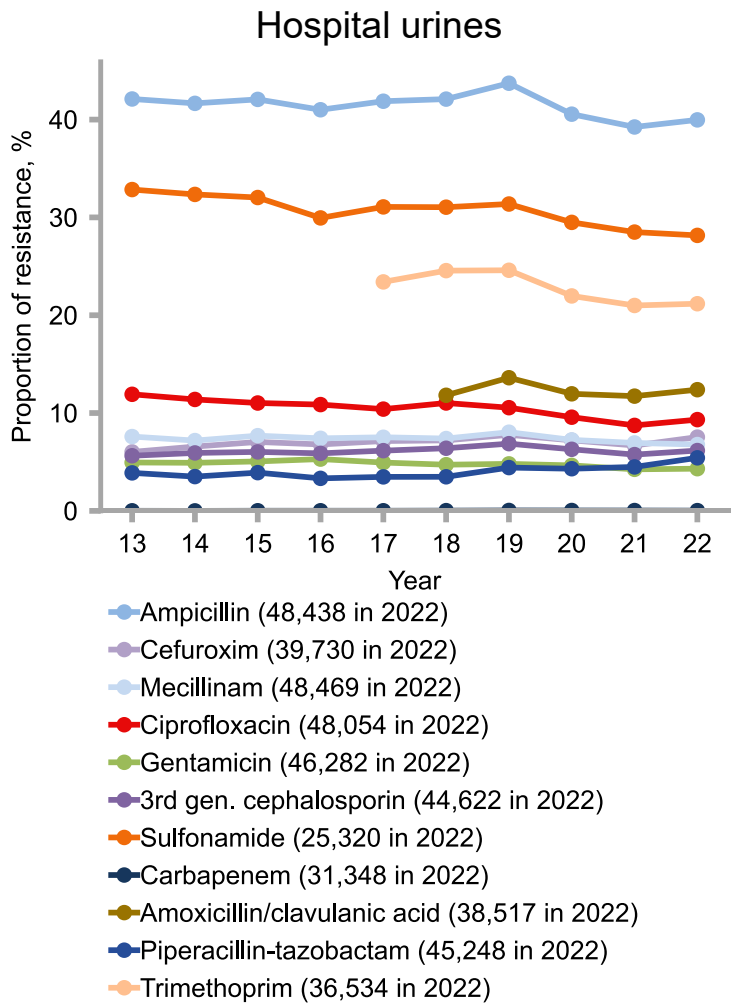
Invasive infections

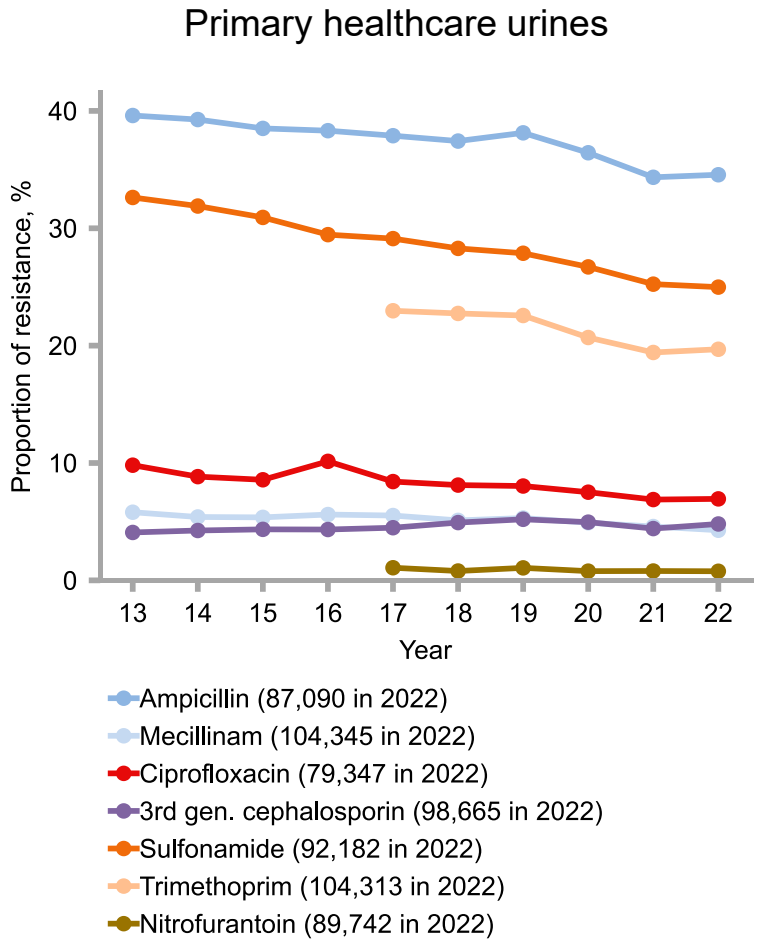




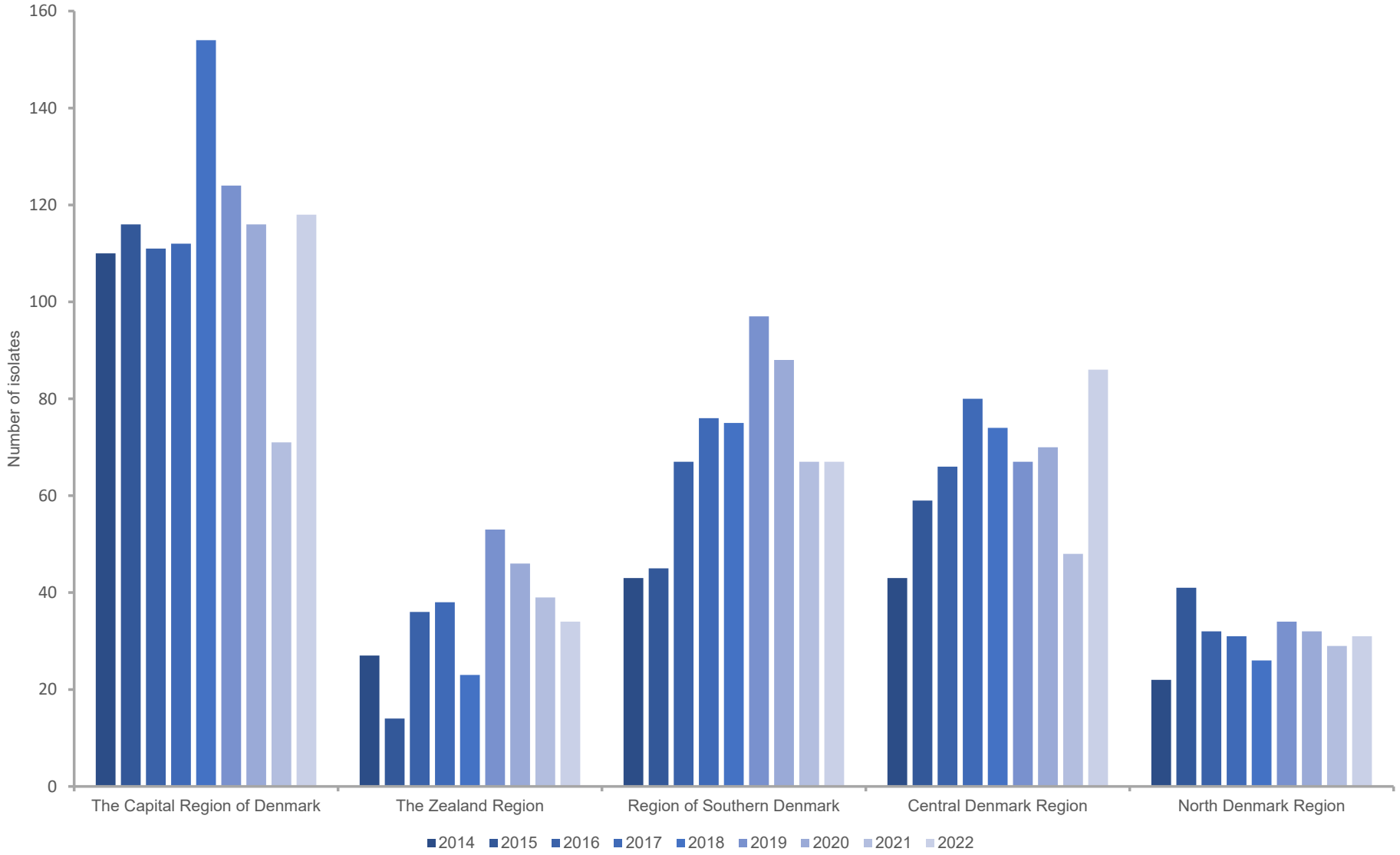
E. coli - invasive infections and urine







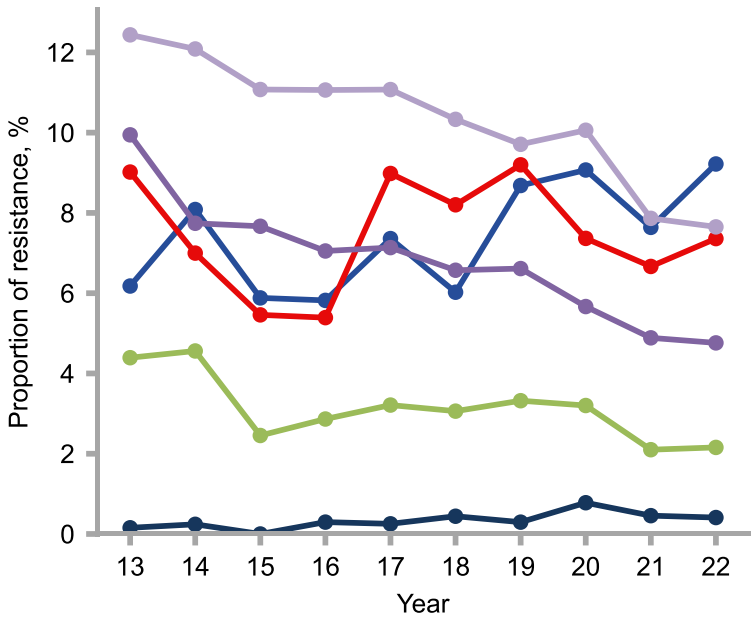
ESBL *E. coli* from invasive infections



K. pneumoniae – invasive infections and urine

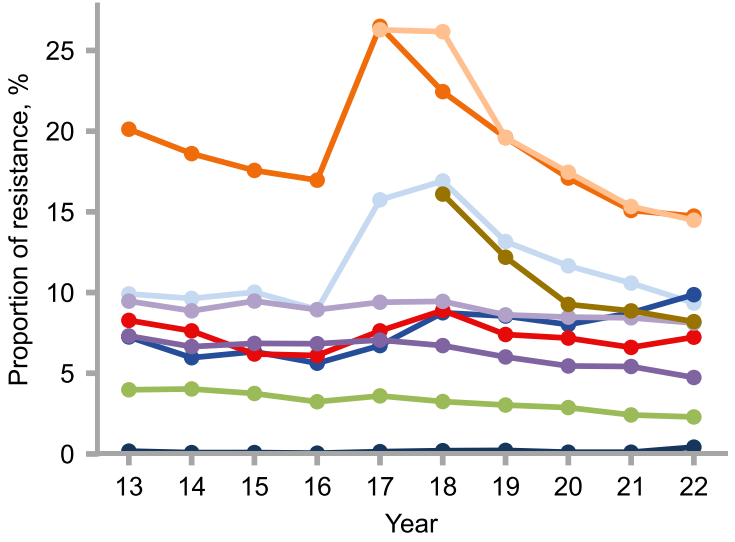
DANMAP

Invasive infections



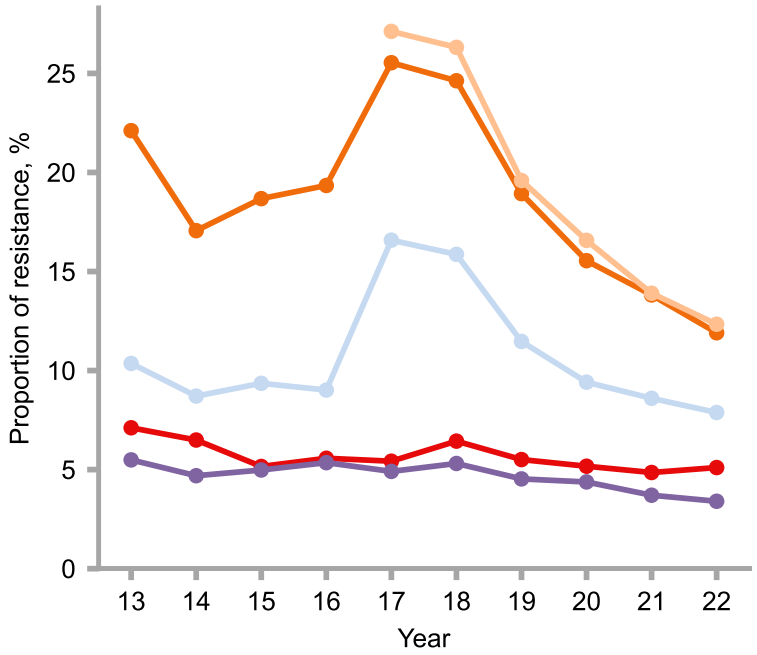
Piperacillin-tazobactam (1,345 in 2022)
Gentamicin (1,344 in 2022)
Ciprofloxacin (1,345 in 2022)
Cefuroxim (1,346 in 2022)
3rd gen. cephalosporin (1,260 in 2022)
Carbapenem (1,219 in 2022)

Hospital urines



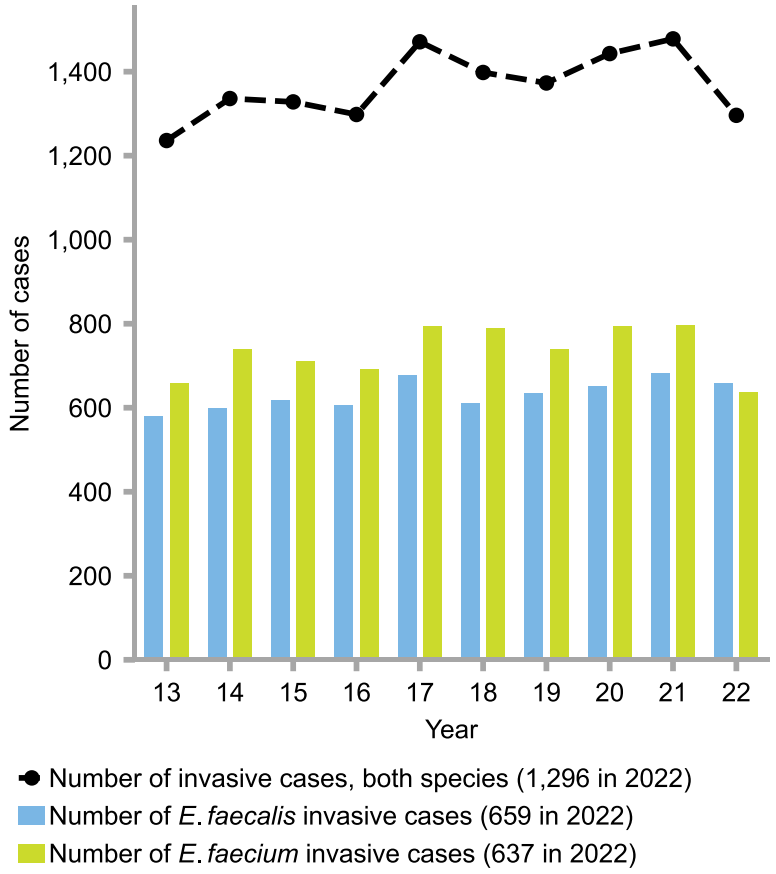
Mecillinam (7,892 in 2022)
Sulfonamide (3,821 in 2022)
Piperacillin-tazobactam (7,784 in 2022)
Ciprofloxacin (7,838 in 2022)
Cefuroxim (6,335 in 2022)
Gentamicin (7,505 in 2022)
3rd gen. cephalosporin (7,136 in 2022)
Carbapenem (4,756 in 2022)
Amoxicillin/clavulanic acid (5,977 in 2022)
Trimethoprim (5,855 in 2022)

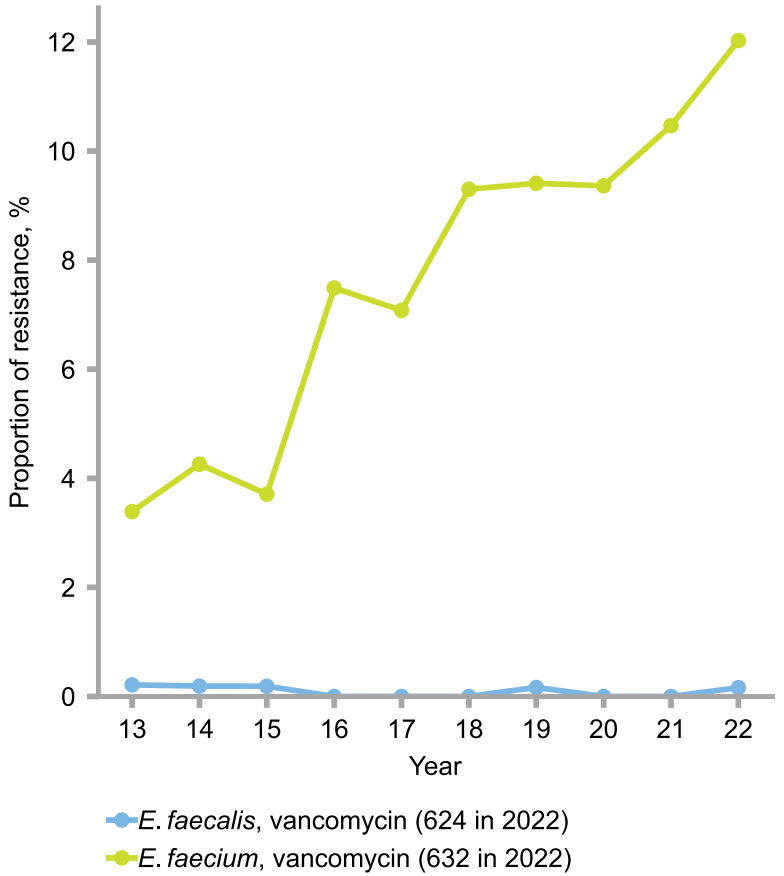
Primary healthcare urines



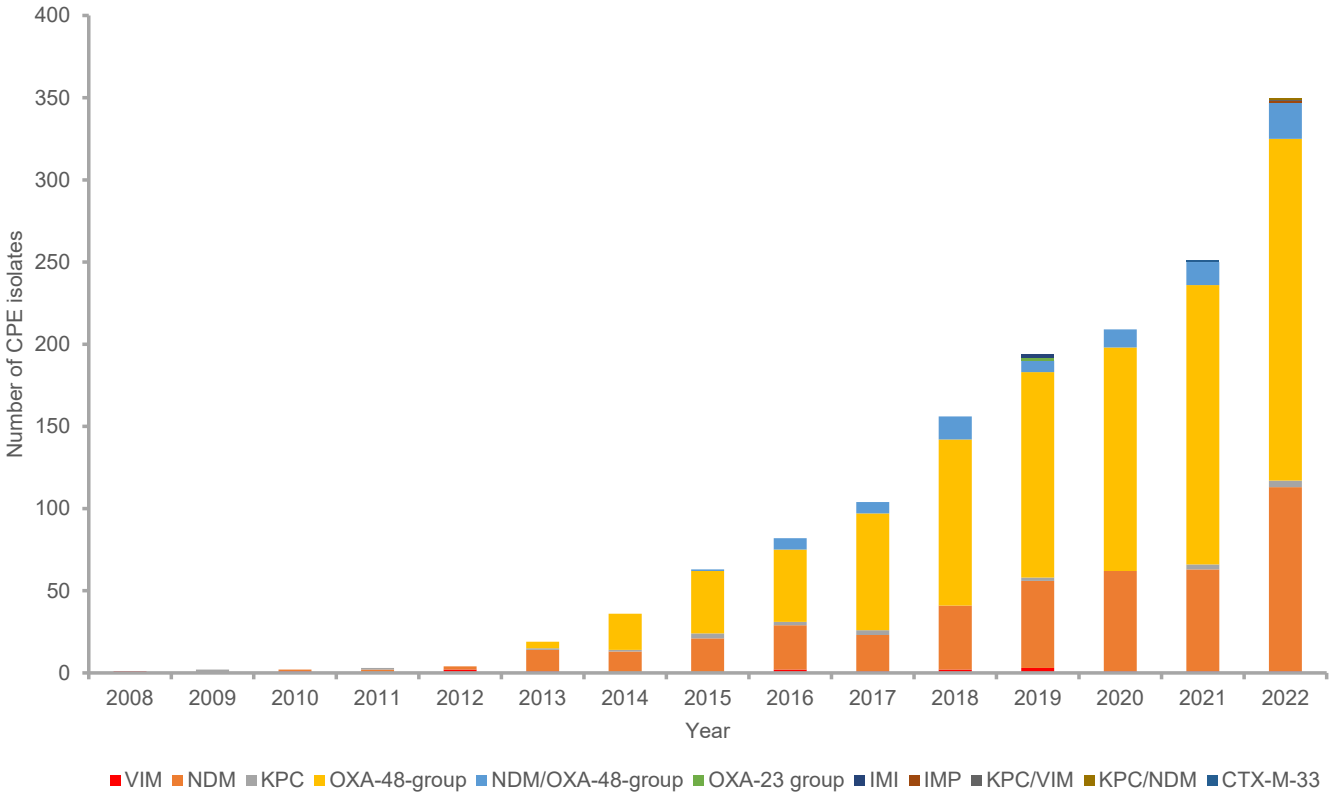
Mecillinam (11,036 in 2022)
Sulfonamide (10,003 in 2022)
Ciprofloxacin (8,484 in 2022)
3rd gen. cephalosporin (10,401 in 2022)
Trimethoprim (11,023 in 2022)

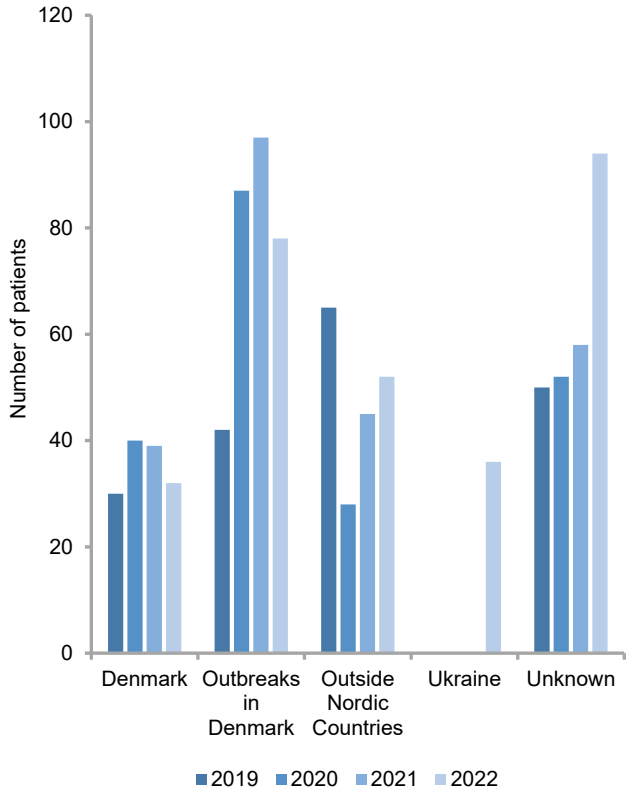
Enterococci and vancomycin resistant enterocci



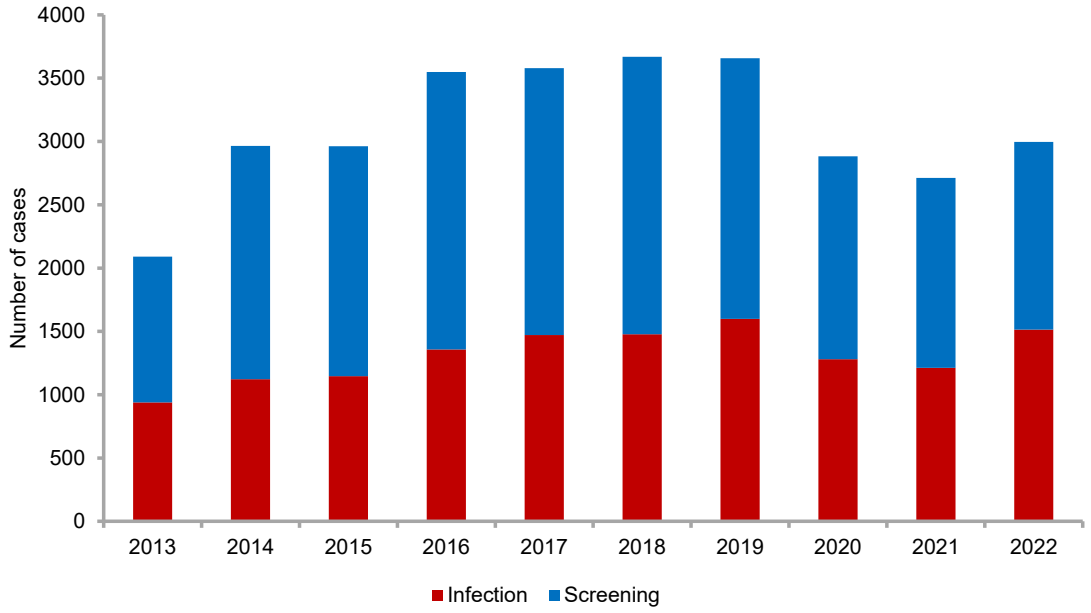


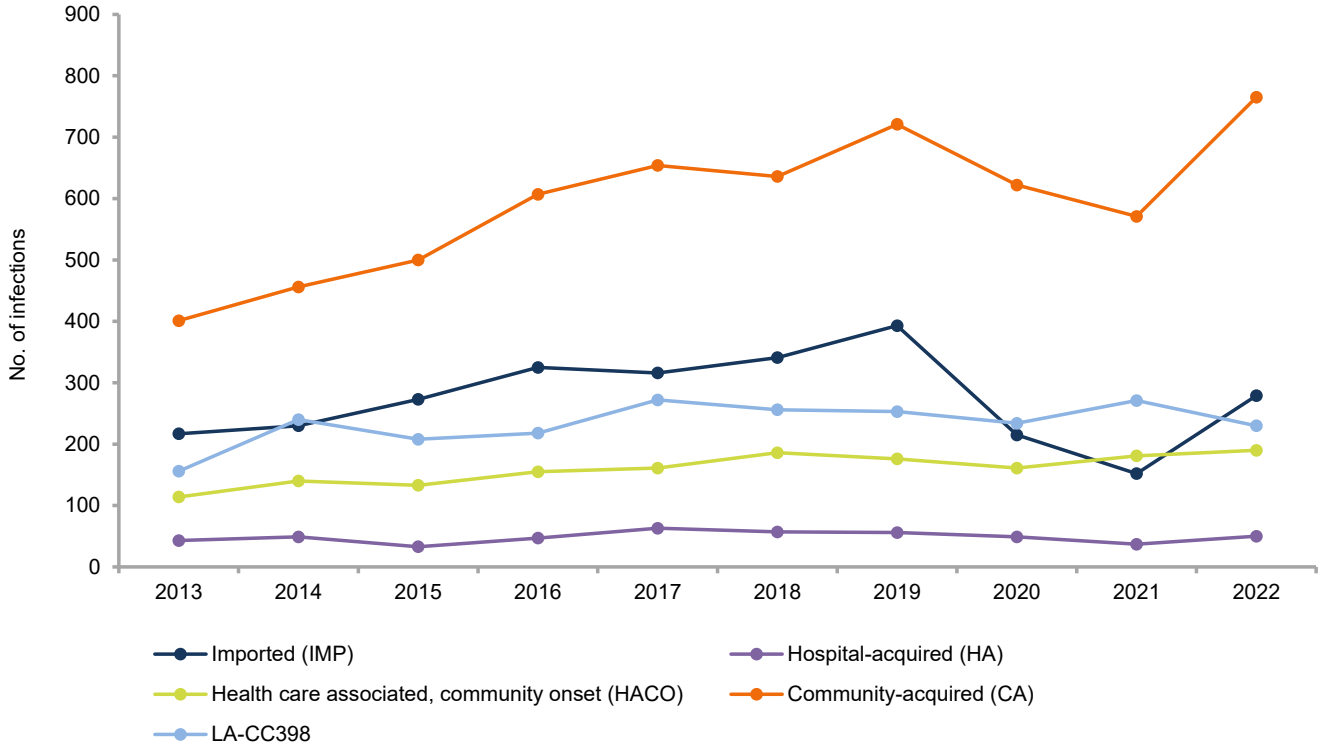
CPO/CPE


Number of CPE isolates
400
350
300
250
200
150
100
50
0
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Year
VIM
NDM
KPC
OXA-48-group
NDM/OXA-48-group
OXA-23 group
IMI
IMP
KPC/VIM
KPC/NDM
CTX-M-33


Number of patients
120
100
80
60
40
20
0
Denmark
Outbreaks in Denmark
Outside Nordic Countries
Ukraine
Unknown
2019
2020
2021
2022

MRSA


4000
3500
3000
2500
2000
1500
1000
500
0
Number of cases
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Infection
Screening


900
800
700
600
500
400
300
200
100
0
No. of infections
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Imported (IMP)
Hospital-acquired (HA)
Health care associated, community onset (HACO)
Community-acquired (CA)
LA-CC398

Main messages

- The incidence of invasive infections appears to have reached a plateau
- After years of decreasing resistance rates, they have now either stabilised or are increasing
  - *K. pneumoniae* resistance towards piperacillin-tazobactam is now nearly 10 %!
- Fewer invasive infections with enterococci, but more resistance towards vancomycin
- Continued increase in number of CPO – largely with unknown epidemiology
- After a decrease in the number of MRSA during the pandemic, numbers are increasing again

Resistance in pathogenic bacteria from pigs

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University of Copenhagen

Svend Haugegaard & Charlotte M. Salomonsen
Veterinary Laboratory
The Danish Agriculture and Food Council

Textboxes

9.1 Antimicrobial resistance in dogs and cats: focus on extended-spectrum cephalosporinase-producing *Escherichia coli* and their resemblance to human clinical isolates

Peter Damborg, Mattia Pirolo, Frank Hansen, Louise Roer, Henrik Hasman and Luca Guardabassi

9.2 Insights into the genetic basis of neomycin resistance in clinical Escherichia coli isolated from pigs

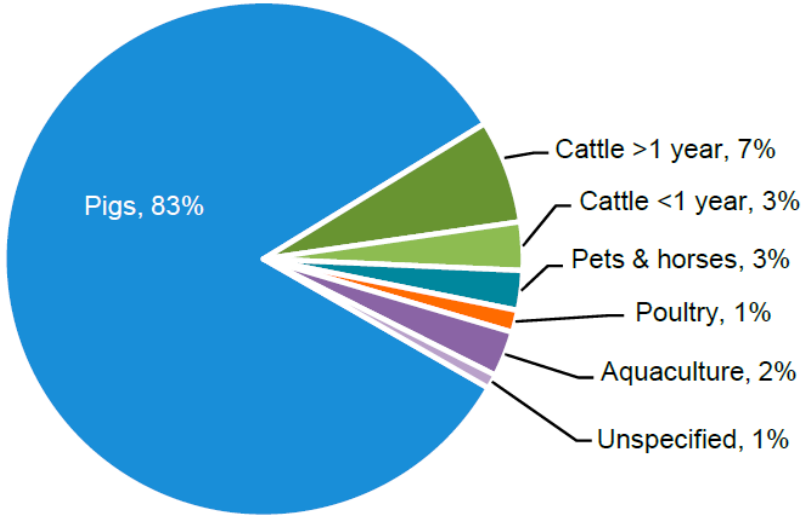
Luca Guardabassi and Peter Damborg, University of Copenhagen, Denmark

9.3 Assessing the burden of Antimicrobial Resistance and Usage in the Global Burden of Animal Disease programme: the start of the Danish case study

Sara Babo Martins, João Sucena Afonso, Christina Fastl, Kassy Raymond, Ben Huntington and Jonathan Rushton

Background

- **Veterinary Laboratory, The Danish Agriculture and Food Council**
  - Receives clinical samples from pigs
  - Performs bacterial culturing, species identification and antimicrobial susceptibility testing (AST)
  - Published in **DANMAP** since 2015
    - *Actinobacillus pleuropneumoniae*
      - Lung infections
    - Haemolytic *Escherichia coli*
      - Post-weaning diarrhoea and other organs
    - *Streptococcus suis*
      - Septicaemia, meningitis, arthritis, endocarditis and other organs



Background

- **Danish Veterinary Consortium**
  - Whole-genome sequencing (WGS)
    - Illumina platforms
  - Identification of resistance genes/mutations
    - ResFinder and PointFinder
  - Comparison of AST and WGS results
    - 1st choice: ECOFFs (EUCAST)
    - 2nd choice: Tentative ECOFFs (EUCAST)
    - 3rd choice: Animal-specific clinical breakpoints (CLSI)
    - 4th choice: Human clinical breakpoints (CLSI)

List of pathogenic bacteria

- *A. pleuropneumoniae* (AST and WGS)
- *Bordetella bronchiseptica* (AST and WGS)
- *Clostridium perfringens* (WGS)
- *Erysipelothrix rhusiopathiae* (WGS)
- Haemolytic and non-haemolytic *E. coli* (AST and WGS)
- *Glaesserella parasuis* (WGS)
- *Klebsiella pneumoniae* (AST and WGS)
- *Salmonella enterica* (AST and WGS)
- *Staphylococcus hyicus* (AST and WGS)
- *S. suis* (AST and WGS)

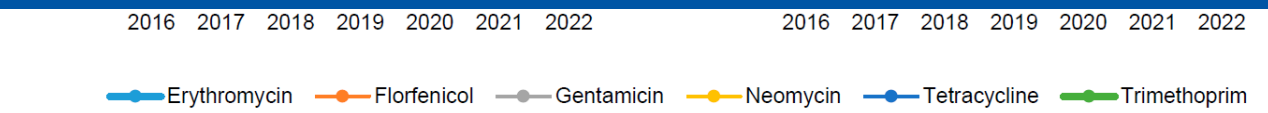
AST

Figure 9.1 Phenotypic antimicrobial resistance among pathogenic bacteria from pigs, Denmark, 2016-2022 DANMAP 2022

Haemolytic *Escherichia coli* Non-haemolytic *Escherichia coli*

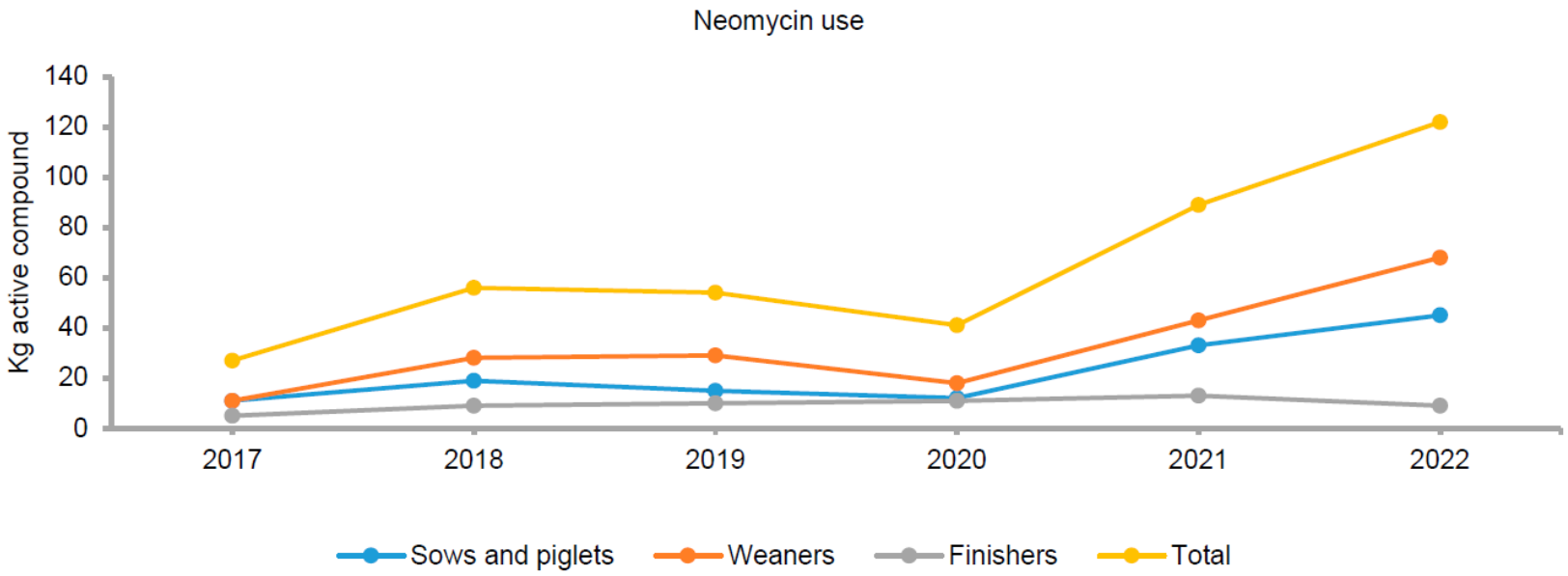
Neomycin resistance in haemolytic *E. coli* increased from 6.9% in 2016 to 43.2% in 2022

Problematic because neomycin is one of only a few drugs recommended in Denmark as first choice for treating *E. coli*-associated post-weaning diarrhoea

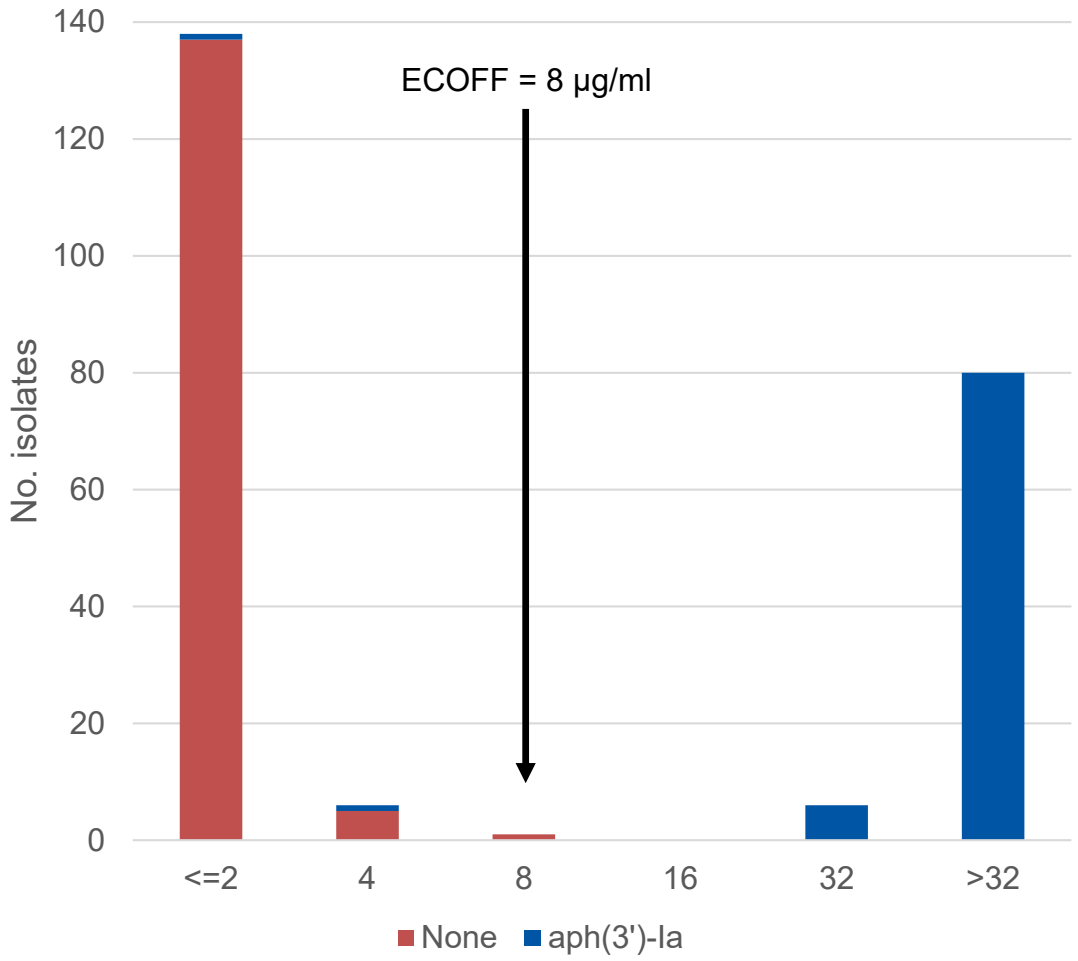


Neomycin resistance in haemolytic *E. coli*

Figure 9.2 Neomycin use in the total pig population and in each age group, Denmark 2017-2022 DANMAP 2022

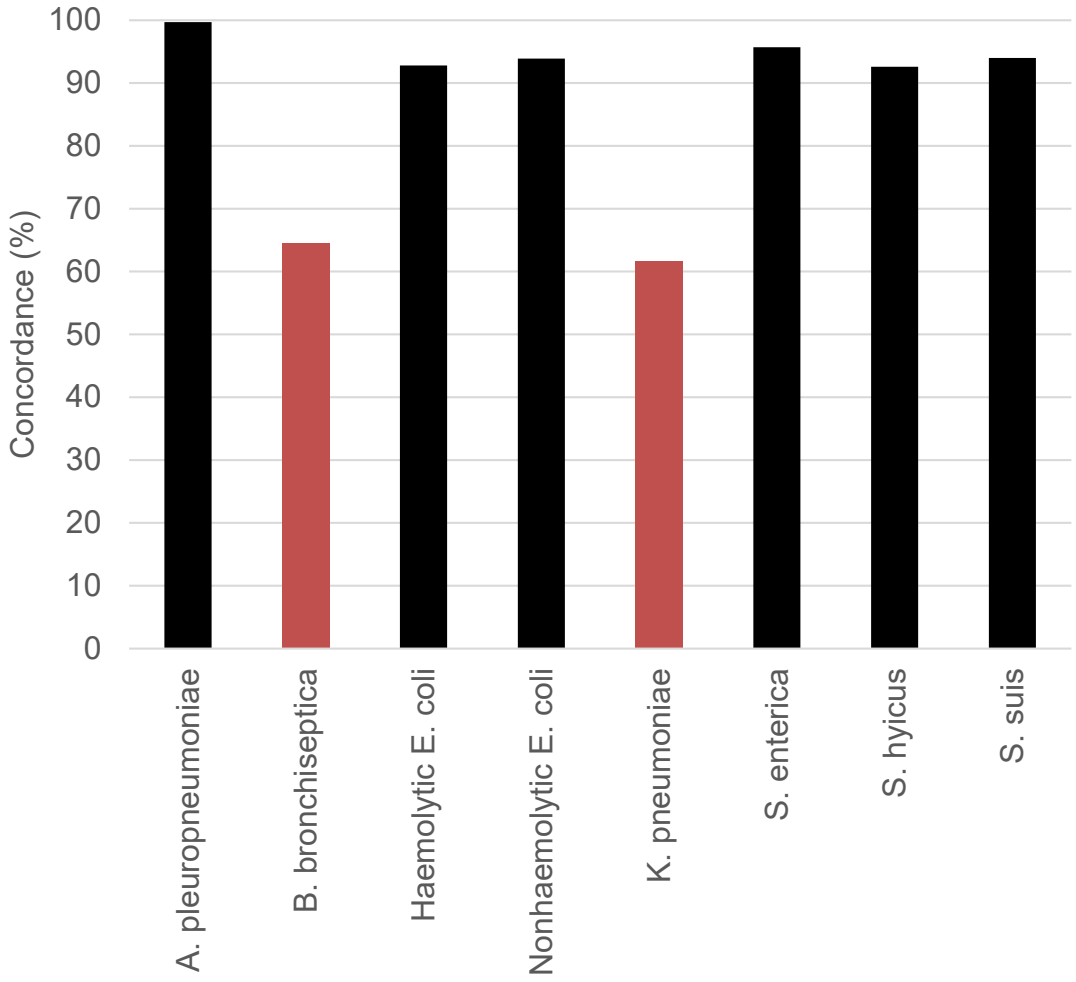


Neomycin resistance in haemolytic *E. coli*



- *aph(3')-Ia* also found in non-haemolytic *E. coli*, *G. parasuis*, *K. pneumoniae* and *S. enterica*
- Haemolytic *E. coli* also displayed medium to high frequencies of resistance to the other first-choice drugs
  - Amoxicillin/clavulanic acid (13.5%)
  - Ampicillin (60.9%)
  - Spectinomycin (57.4%)
  - Trimethoprim/sulfamethoxazol (54.8%)
  - Streptomycin (78.0%)

AST vs. WGS



- All *B. bronchiseptica* isolates were phenotypically resistant but genotypically susceptible to ampicillin
  - Wrong animal-specific clinical breakpoint or presence of unknown resistance genes/mutations
- All *K. pneumoniae* isolates were phenotypically susceptible to cefotaxime but harboured mutations in *ompK36*/*ompK37* associated with resistance cephalosporins
  - Wrong ECOFF or single point mutations insufficient for resistance

Resistance genes of human relevance

- Linezolid
  - *cfr*(B) and *cfr*(E) were present in 1.8% and 3.6% of the *C. perfringens* isolates
  - *optrA* was present in 1.4% of the *S. suis* isolates
- 3rd, 4th and 5th generation cephalosporins
  - $bla_{\text{TEM-169}}$ gene was present in 1.9% of the non-haemolytic *E. coli* isolates
  - $bla_{\text{SHV-27}}$ was present in 6.3% of the *K. pneumoniae* isolates
- Carbapenems and colistin
  - No resistance genes were detected

Future work

- Multidisciplinary analyses to investigate discordances between AST and WGS
  - Identification of new resistance genes/mutations
  - Establishment/evaluation of ECOFFs/animal-specific clinical breakpoints
- Bioinformatic analyses to investigate spread of resistance genes and pathogenic bacteria within and between animal and human populations

www.vetssi.dk/

Thank you for your attention!

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Contributing authors to chapters

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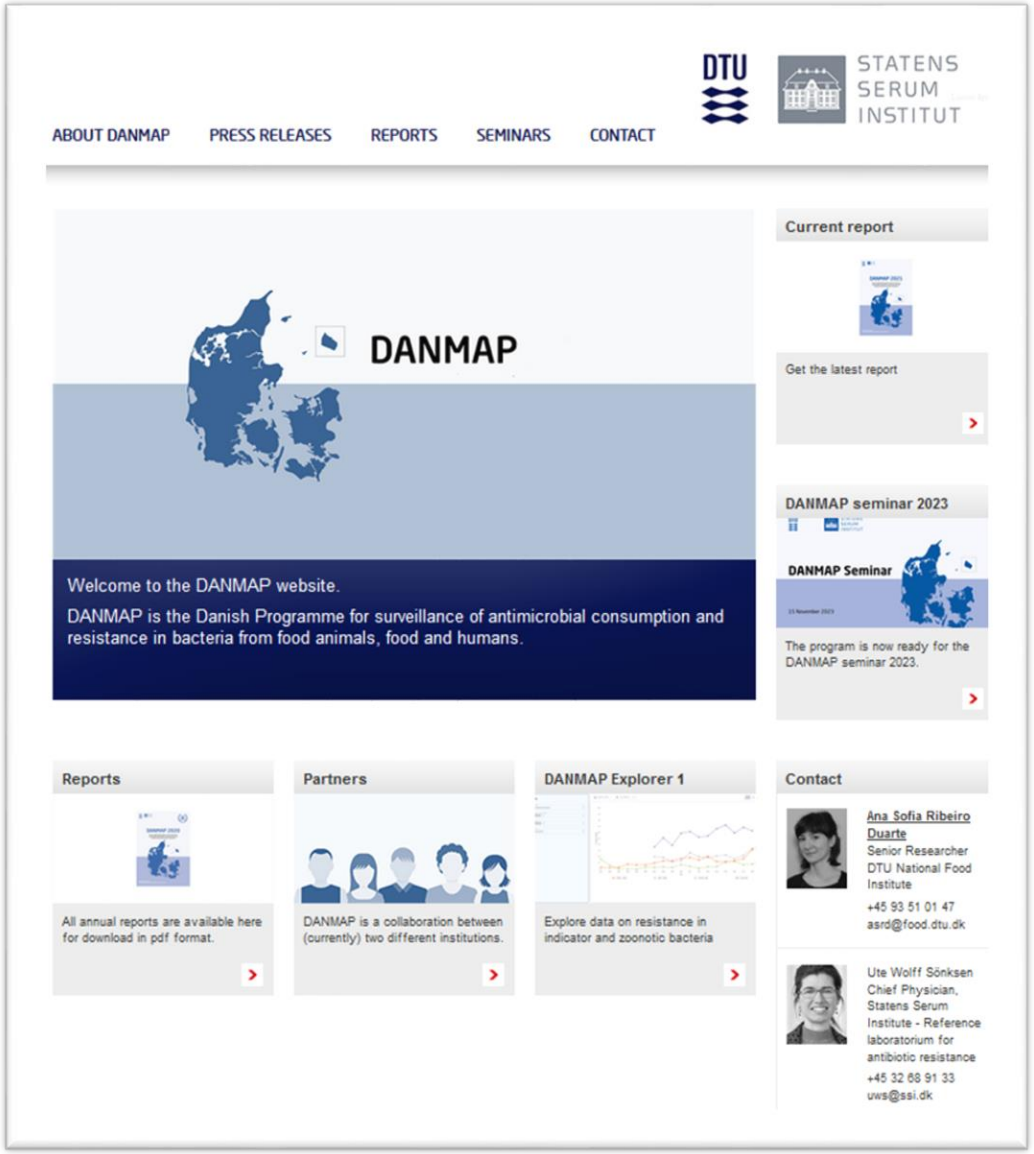

Thank you for your attention